UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

BOEHRINGER INGELHEIM PHARMACEUTICALS INC., BOEHRINGER INGELHEIM INTERNATIONAL GMBH, BOEHRINGER INGELHEIM CORPORATION, and BOEHRINGER INGELHEIM PHARMA GMBH & CO. KG,

Plaintiffs,

v.

HEC PHARM CO., LTD., HEC PHARM USA, MYLAN PHARMACEUTICALS INC., MYLAN INC., MYLAN LABORATORIES LIMITED, ACCORD HEALTHCARE, INC., AUROBINDO PHARMA LIMITED, AUROBINDO PHARMA USA, INC., DR. REDDY'S LABORATORIES, LTD., DR. REDDY'S LABORATORIES, INC., ZYDUS PHARMACEUTICALS USA, INC., CADILA HEALTHCARE LTD., MSN LABORATORIES PRIVATE LIMITED, MSN PHARMACEUTICALS, INC., PRINSTON PHARMACEUTICAL INC., INVAGEN PHARMACEUTICALS INC., SUN PHARMACEUTICAL INDUSTRIES LTD., SUN PHARMA GLOBAL FZE, and TEVA PHARMACEUTICALS USA, INC.,

Defendants.

Civil Action No:
15-cv-5982 (PGS)(TJB)

MEMORANDUM

SHERIDAN, U.S.D.J.

This is a consolidated a patent infringement action brought by Boehringer Ingelheim Pharmaceuticals Inc., Boehringer Ingelheim International GmbH, Boehringer Ingelheim Corporation, and Boehringer Ingelheim Pharma GmbH & Co. KG (collectively, "Boehringer" or "Plaintiffs") against Mylan Pharmaceuticals Inc., Mylan Inc., and Mylan Laboratories Limited

("Mylan") and Aurobindo Pharma Limited and Aurobindo Pharma USA, Inc. ("Aurobindo) (all defendants collectively, "Defendants")[1] for filing an Abbreviated New Drug Application ("ANDA") with the Food & Drug Administration ("FDA"), pursuant to 21 U.S.C. § 355(b)(2) (Hatch-Waxman Act), for approval to engage in the commercial manufacture, use or sale of a generic version of Tradjenta® and Jentadueto®. *See* 35 U.S.C. § 271 (Patent Act).

Tradjenta® (linagliptin) and Jentadueto® (linagliptin + metformin) are used to manage type 2 diabetes. Boehringer listed several patents for both Tradjenta® and Jentadueto® in the Orange Book. These included U.S. Patent Nos. 8,178,541 ("'541 patent"), 8,673,927 ("'927 patent) and 9,173,859 ("'859 patent"). These patents "generally describe methods to treat diabetes that involve the use of a compound known as linagliptin, alone or in combination with various other antidiabetic treatments [such as metformin]." (Tr. 480:20-24 (Accili)). While Aurobindo applied for an ANDA only with regards to Tradjenta®, Mylan applied for approval for both Tradjenta® and Jentadueto®. Defendants seek to start production of the generic products following expiration of Boehringer's U.S. Patent No. 7,407,955 ('955), U.S. Patent 8,119,648 ('648), and the '541 patent. Before the Court are claims 7, 9, 15, 17, 19, 25, and 26 of the '927 patent, and claims 1, 14, 15, 20, and 21 of the '859 patent, (all collectively, the "Asserted Claims" of the patents-in-suit). Claims 14 and 15 of the '859 patent are collectively referred to herein as the "tablet claims," as they deal with the formation of the drug; and the remaining Asserted Claims are referred to as the "method claims," as they deal with the administration of the drug.

Boehringer initiated this suit against Defendants alleging that Defendants' requests to market the generic version of Tradjenta® and Jentadueto® infringed upon Boehringer's rights granted under the '927 and '859 patents, because the proposed labels will induce physicians to

[1] Mylan and Aurobindo are the only remaining Defendants in this action.

administer linagliptin in combination with metformin in a specific dosage ("Combination Therapy[2]").

In response, Defendants argue that the asserted claims 7, 9, 15, 17, 19, 25, and 26 in the '927 patent and the asserted claims 1, 14, 15, 20, and 21 in the '859 patent are prima facie invalid for obviousness-type double patenting, because these claims are a recitation of the claims found in the '541 patent. Defendants further argue that the asserted claims are prima facie invalid as obvious, as the asserted claims had been previously disclosed by prior art. At trial, Defendants, bearing the burden to invalidate the asserted claims of the '927a nd '859 patents, presented expert evidence to show that the asserted claims are invalid as noted above. The experts were Joshua Cohen, M.D., Domenico Accili, M.D., George M. Grass, Ph.D., David Blackburn, Ph.D., and Christian Wolf, Ph.D.

In response, Boehringer defended the patents by arguing the '541 claims are patentably distinct. Further, Boehringer argues that the asserted claims are not invalid for obviousness as Defendants have failed to show that a person of ordinary skill in the art ("POSA") would have been directed to prior art, that a POSA would have been motivated to select specific dosages of linagliptin, and that a POSA would have been motivated to combine linagliptin and metformin. Additionally, Boehringer argues that secondary considerations support a non-obvious finding. In order to advance these positions, Boehringer relied on the following witnesses and experts: Michael G. Mark, Ph.D., M. James Lenhard, M.D., Y.W. Francis Lam, Ph.D., William L. Jorgensen, Ph.D., and Steven Schwartz, Ph.D.

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[2] Dr. Accili, Defendant's expert, explained that "combination therapy is when you mix more than one drug for the purpose of treating diabetes." (Tr. 496:14-19) (Accili)).

At the end of the trial, the parties submitted proposed findings of fact and conclusions of law, followed by reply papers.

I

A. The Parties

Plaintiff Boehringer is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business in Ridgefield, Connecticut. (Stip. of Facts, ECF No. 539-1 at ¶ 1). Plaintiff Boehringer Ingelheim International GmbH ("BII") is a private limited liability company organized and existing under the laws of Germany, having a principal place of business in Ingelheim, Germany. (*Id.*) Plaintiff Boehringer Ingelheim Pharma GmbH & Co. KG ("BIPKG") is a limited liability partnership organized and existing under the laws of Germany, having a principal place of business in Ingelheim, Germany. (*Id.*) Plaintiff Boehringer Ingelheim Corporation ("BIC") is a corporation organized and existing under the laws of Nevada, having a principal place of business in Ridgefield, Connecticut. (*Id.*) BIPI, BII, BIPKG and BIC are collectively referred to as "Plaintiffs" or "Boehringer."

Defendant Mylan Pharmaceuticals Inc. ("Mylan Pharms") is a corporation organized and existing under the laws of the State of West Virginia, having a principal place of business in Morgantown, West Virginia. (*Id.*) Defendant Mylan Inc. is a corporation organized and existing under the laws of the State of Pennsylvania, having a principal place of business in Canonsburg, Pennsylvania. (*Id.*) Defendant Mylan Laboratories Limited ("Mylan Labs") is a corporation organized and existing under the laws of India and has a principal place of business in Hyderabad, India. (*Id.*) Mylan Pharms, Mylan Inc., and Mylan Labs are collectively referred to hereinafter as "Mylan."

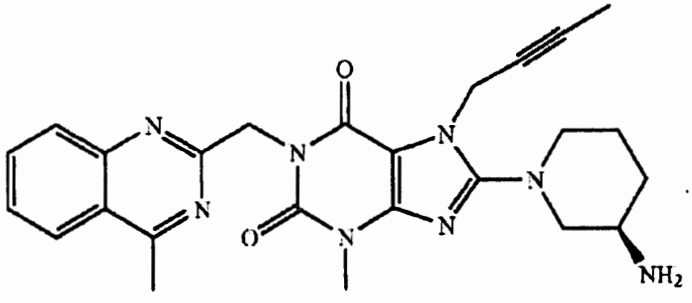
Defendant Aurobindo Pharma Limited ("Aurobindo Ltd.") is a corporation organized and

existing under the laws of India, with a registered place of business in Andhra Pradesh, India. (*Id.*) Defendant Aurobindo Pharma USA, Inc. ("Aurobindo USA") is a corporation organized and existing under the laws of the State of Delaware and has a principal place of business in Dayton, New Jersey. (*Id.*) Aurobindo Ltd. and Aurobindo USA are collectively referred to as "Aurobindo."

B. The Drugs

1. Tradjenta ®

Boehringer holds an approved New Drug Application (No. 201280) ("NDA") for linagliptin, for oral use in 5mg dosages, which is marketed and sold under the trade name Tradjenta®. (Stip. Facts, ECF No. 539-1, at ¶ 35.) Tradjenta® was first approved by the FDA in 2011, and contains 5mg of linagliptin as its active ingredient. (*Id.* at ¶¶ 36-37). Linagliptin is a Dipeptidyl peptidase-4 (DPP-IV) inhibitor, and is used to treat type 2 diabetes mellitus (hereinafter "type 2 diabetes"). (*Id.* at ¶ 46). Linagliptin has the following chemical structure:



Among others, Boehringer listed U.S. Patent Nos. '541, '927, and '859 in the FDA's Orange Book for Tradjenta ®. (*Id.* at ¶ 57).

2. Jentadueto ®

Boehringer holds an approved NDA (No. 201281) for linagliptin and metformin hydrochloride tablets, for oral use in 2.5mg/500 mg, 2.5mg/850 mg, and 2.5/1000 mg dosages, which is marketed and sold under the trade name Jentadueto ®. (*Id.* at ¶ 47). Jentadueto® was

first approved by the FDA in 2012, and contains 2.5 mg linagliptin/500 mg metformin hydrochloride, 2.5 mg linagliptin/850 mg metformin hydrochloride, or 2.5 mg linagliptin/1000 mg metformin hydrochloride as its active ingredients. (*Id.* at ¶ 49). Jentadueto® is used to improve glycemic control in adults with type 2 diabetes. (*Id.* at ¶ 56).

Among others, Boehringer listed patent Nos. '541, '927, and '859 in the FDA's Orange Book for Jentadueto®. (*Id.* at ¶ 58).

3. Aurobindo's Generic

Aurobindo submitted ANDA No. 208415 to the FDA, identifying Tradjenta® and seeking approval to market linagliptin, for oral use, in 5 mg dosages. (*Id.* ¶ 60). Aurobindo included in ANDA No. 208415 a Paragraph IV certification. (Def.'s Proposed Findings of Fact ("PFoF"), ECF No. 597 at ¶ 129). Arbundo later submitted an amendment to ANDA No. 208415 which included paragraph IV certifications as to the '859 patent. (*Id.*)

4. Mylan's Generic

Mylan submitted ANDA No. 208431 to the FDA, identifying Tradjenta® and seeking approval to market linagliptin, for oral use, in 5 mg dosage (the "Mylan Generic"). (Stip. Facts at ¶ 67.) Mylan also submitted ANDA No. 208430 to the FDA, identifying Jentadueto® and seeking approval to market linagliptin and metformin, for oral use, in 2.5 mg/500 mg, 2.5 mg/850 mg, and 2.5 mg/1000 mg dosages (the "Mylan Generic Combination"). (*Id.* at ¶ 68.) Included with ANDA No. 20831 was a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), [redacted] (*Id.* at ¶ 69.) Additionally, Mylan included in ANDA No. 208430 paragraph IV certifications [redacted] (*Id.* at ¶¶ 69-70.)

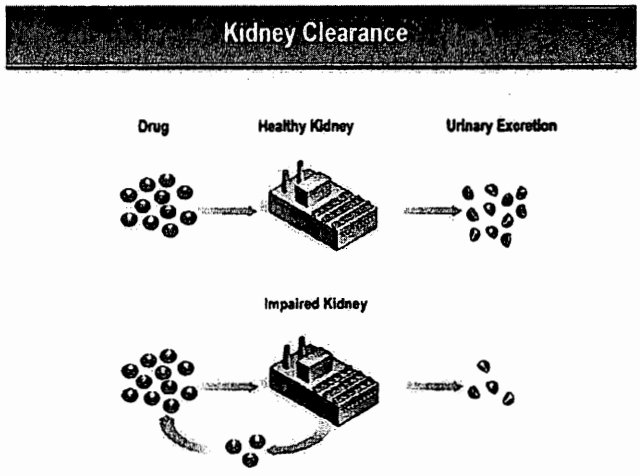
5. Development of Tradjenta® and Jentadueto®

a. Linagliptin

Tradjenta® and Jentadueto® are two drugs used to manage type 2 diabetes. Diabetes is a chronic disease, and is characterized by elevated levels of glucose and blood sugar. (*See* Tr. 287:15-16 (Lenhard); Tr. 485:7-8 (Accili)). Insulin is the hormone that regulates glucose sugar levels. (Tr. 485:22-25 (Accili)). Insulin resistance is the "cause of diabetes;" and an individual with insulin resistance has difficulty keeping their glucose levels within normal range. (Tr. 486:1-2 (Accili)). Dr. Accili explained, "the liver makes glucose, for example, while we eat[;] the reason we don't go into low blood sugar when we do not eat is the liver takes up the function of making glucose. [If] this process in diabetes is uncontrolled, . . . it makes [excessive] glucose." (Tr. 489:16-23) (Accili)).

Diabetes causes both microvascular and macrovascular complications. Microvascular complications can occur when diabetes affects small blood vessel, which can cause damage to the eyes, heart, nerves, and kidneys. (Tr. 289:8-17 (Lenhard)). Macrovascular complications can occur when diabetes affects large blood vessels, and can cause heart attack, stroke, blood clots and blockages to the lower extremities. (Tr. 289:8-17 (Lenhard)). Renal impairment and impaired kidneys affect how specific drugs act in the body. Boehringer's expert Dr. Lenhard testified that "[m]any drugs are excreted from the body by way of the kidney after they serve their therapeutic use, they're filtered from the blood by the kidney . . . if the kidney is functioning normally . . ., then the drug is excreted in its entirety." (Tr. 854:10-14 (Lenhard)). However, "[i]f the kidney is impaired in some way, then the drug may not be cleared to the same extent[,] leading to a build-up of the drug [in the body]." (Tr. 854:14-16 (Lenhard)). After excretion through the kidney, drugs then go through urinary excretion. (Tr. 854:20-22 (Lenhard)). Patients that experience renal

impairment are limited in which drugs they may take to treat their type 2 diabetes. (Pl.'s Findings of Fact ("PFoF"), ECF No. 594 at ¶ 73). The following graphic displays the issues related to renal impairment and drug clearance:



(PDX-6.11).

Drugs used to treat type 2 diabetes are cleared primarily through the kidney, thus, renal impairment is a primary concern for type 2 diabetes patients. For example,"[f]ollowing oral administration [of metformin, a first-line drug to treat type 2 diabetes], approximately 90% of the absorbed drug is eliminated via the renal route within the first 24 hours." (DTX-39.3). For this reason, metformin is "contraindicated in patients with: renal disease or renal dysfunction . . . which may also result from conditions such as cardiovascular collapse (shock), acute myocardial infarction, and septicemia," and the prescribing label for metformin cautions against the use of metformin in renally impaired patients. (DTX-39.14.) Other DPP-IV inhibitors also clear primarily through the kidney: Sitagliptin (79% cleared through the kidney); Saxagliptin (24%, 36% and 45% cleared through the kidney); Alogliptin (76% cleared through the kidney); and Vildagliptin (85% cleared through the kidney). (PFoF, ECF No. 594 at ¶ 806).

Dr. Accili testified that patients suffering from type 2 diabetes have their renal functions tested about once a year. (Tr. 1338:1-10) (Accili)). Dr. Accili explained: "So, in all these patients the main reason you test renal function is because of their diabetes, not because of the drug they're on . . . [, but because] kidney disease . . . [is an] important component of diabetes. And so most professional associations recommend that patients be tested yearly, so you have to do that as a baseline." (Tr. 1338:16-24) (Accili)). To test a renal function, physicians conduct a blood test that measures a patient's renal impairment. (Tr. 1339:12-16 (Accili)).

The dosage of a drug affects renal excretion, depending on "how quickly the drug builds up in the bloodstream and . . . whether there is a reason to threshold for renal excretion." (Tr. 1345:21-23 (Accili)). Accordingly, patients with renal impairment require dose adjustments, which starts with giving a patient half the required dose of a drug. (Tr. 1337:6-12 (Accili)). The further the renal impairment progresses, the more the dose is adjusted; for example, if the starting dose is 100mg, a physician would cut the dose in half to 50mg, and then eventually reach 25mg of a drug. (Tr. 1337:19 to 23) (Accili)).

Common therapies to treat type 2 diabetes included metformin, insulin sensitizers, insulin secretagogues, glucose absorption inhibitors, GLP-1 receptor agonists, and DPP-IV inhibitors. (Tr. 488:1 to 492:6 (Accili)). The American Diabetes Association ("ADA") publishes guidelines for the treatment of diabetes, and these guidelines recommend that patients be treated first with metformin monotherapy. (Tr. 291:2-22 (Lenhard); *see also* Tr. 492:25 to 493:2 (Accili)). At trial, Dr. Accili explained that "metformin . . . appeared in the British formulary in . . . 1958, 60 years ago. However, there are reports even from the 1940s saying that it lowered glucose. Metformin is a plant extract essentially, so it's been around for a long time." (Tr. 493:7-11 (Accili)). Metformin was approved by the FDA in 1995. (Defs. PFoF, ECF No. 597, at ¶ 71). Accordingly,

Dr. Dugi opined that "[M]etformin was available commercially on the market for a long time with an FDA approved label. Physicians knew how to use metformin." (Tr. 1458:13-1459:15) (Dugi)). After measuring a patients HbA1c, if it is shown that metformin treatment is not successful on its own, a physician would add a second drug to the treatment.[3] (Tr. 291:12-18) (Lenhard)). The ADA guidelines recommend comprising "two drug therapy [with] metformin and life-style changes with one of several different drugs added to that." (Tr. 291:23-292:2 (Lenhard)). For example, two drug therapy can include metformin and a DPP-IV inhibitor. (T2. 292:3-8) (Lenhard)).

During the 1990s, Boehringer biologist Dr. Michael Mark determined "there [was] . . . a high therapeutic need for novel treatments in diabetes, because none of the treatments at that point in time [were] able to reduce the progression of the disease." (Tr. 39:24 to 40:2 (Mark)). Accordingly, Boehringer focused on developing DPP-IV inhibitors as a potential treatment for type 2 diabetes. (Tr. 42:7-8) (Mark)). DPP-IV inhibitors work to allow Glucagon-like peptide-1 ("GLP-1") to function correctly. GLP-1 is a "very important hormone which . . . [controls] the glucose levels of the human being, . . . [and is] able to increase the insulin secretion." (Tr. 42:20-22 (Mark)). Dr. Mark explained that "[A]fter someone eats a meal, their blood glucose level goes up," and "then the body releases [] [GLP-1]." (Tr. 42:23-25 (Mark)). GLP-1 then "signal[s] . . . the body to release insulin to address the higher glucose level," and "insulin is able to reduce glucose levels." (Tr. 43:3 to 5 (Mark)). In contrast, DPP-IV is the enzyme that inactivates GLP-1, thus making it unfunctional. (Tr. 43:8-9 (Mark)). DPP-IV inhibitors, like linagliptin, block this

[3] HbA1c is the measurement of glucose in the blood. (*See* Tr. 40:12-20 (Mark)).

function of the DPP-IV enzyme, thus allowing "longer and higher [GLP1-] levels existing" in the blood, which in turn allows "the body [to] secret[e] insulin." (Tr. 43:12-17) (Mark)).

Boehringer first developed a proprietary assay to search for DPP-IV inhibitors, and after screening approximately 500,000 compounds, identified a "double digit" number of "hits." (Tr. 47:6-22) (Mark)). The proprietary assay was then "adapted for [] high throughput screening" and using this, Boehringer screened approximately 500,000 compounds, comprising of "all the compounds which were existing in Boehringer [] at that point in time." (Tr. 45:8-24 (Mark).)

Next, Boehringer began to structurally modify the hits in an attempt to identify "novel molecules . . . with different features and different results." (Tr. 48:6-20 (Mark)). Boehringer estimates it synthesized approximately 1,500 molecules over a two year period. (Tr. 48:21 to 49-2 (Mark)). Based on *in vivo* and *in vitro* assays, Boehringer selected BI-1344 for development; however, in developing that compound, Boehringer discovered "negative safety signals, and . . . had to discontinue the further development of BI-1344." (Tr. 50:13-25; 51:9-13 (Mark)). Thereafter, Boehringer identified BI-1356 (now known as linagliptin, (Tr. 51:22-25 (Mark)), and conducted *in vivo* and *in vitro* assays, which did not exhibit the same negative safety signals as BI-1344 during development. Linagliptin was ultimately approved by the FDA for use in treating patients with type 2 diabetes. (Tr. 54-21 to 55-3 (Mark)).

After identifying linagliptin, Boehringer tested the compound "in various animal models and in various species," and identified a dose range of one to three milligrams. (Tr. 55:9-19 (Mark)). This dose range equates to between 50 and 200 milligrams in human dosages. (Tr. 55:9-19 (Mark)). Using this estimate, Boehringer conducted a human trial (*in vivo*) on non-type 2 diabetic, healthy volunteers, to start with a dose of about 5 mg as a subtherapeutic dose, which is a dose "showing no efficacy . . . meant as a safety measure to really start in the first human exposure

relatively low and safe." (Tr. 56:14 to 57:2) (Mark)). Boehringer's expected therapeutic dose was between 50 and 200mg per day. (Tr. 62:6-7) (Mark)). As a result of this clinical study, Boehringer determined that "there was a greater than 60% DPP-IV inhibition" after twenty-four hours with a 5 mg dose. (*Id.* at ¶ 90). Additionally, Boehringer found that in the 2.5 and 5 mg doses, only a small amount was excreted via the kidney. (Pl.s' FoF, ECF No. 594, at ¶ 811; Tr.64:15-21 (Mark)). Linagliptin is instead "excreted through the intestine and the liver and not through the kidney[s] like the other DPP-IV inhibitors." (Tr. 902:12-14 (Lenhard)). Thus, linagliptin's "renal excretion as percentage of dose of linagliptin" increases at a higher dose and decreases at a lower dose. (Pl.s' PFoF, ECF No. 594, at ¶ 91).

After the results of the first clinical study, Boehringer narrowed the dose range to 1, 2.5, 5 and 10 mg, and conducted subsequent clinical studies, this time on individuals with type 2 diabetes. (Pl.s' FoF, ECF No. 594, at ¶¶ 92-94. These studies showed that linagliptin is "safe and well tolerated" in "oral doses of 2.5, 5 and 10mg", and the "maximum inhibitory effect" approached the 5 mg dose. (*Id.* at ¶¶ 96-100). They also showed that "[r]enal excretion of [linagliptin] accounted for about 3% of the total clearance." (Pl.s' FoF, ECF No. 594, at ¶ 97). Because most type 2 diabetic patients suffer from renal impairment, "they have a reduced kidney function, and therefore any compound which is eliminated via the kidney would additionally put [a] burden [on] the kidney which is malfunctioning in these patients" thus, the lower the amount to pass through the kidney, the lower the burden on the kidney. (Tr. 65:1-8; 74-20 (Mark)).

Around this time, Boehringer began to investigate linagliptin's effect on HbA1c. (Pl.s' FoF, ECF No. 594, at ¶ 99). If there is a significant reduction in a HbA1c value, there is an improvement in glycemic control. (Tr. 75:21-23 (Mark)). Dr. Mark explained, "HbA1c is the final marker which is needed for regulatory bodies, but it's also used for the doctor, to really see whether

there is a change in the glycemic control." (Tr. 74:22-24 (Mark)). Boehringer found a "a statistically significant reduction of HbA1c," and proceeded to file the '927 and '859 patents, which have the earliest effective filing date of May 4, 2006. (*Id.* at ¶¶ 101-102). After filing the '927 and '859 patents, Boehringer continued to perform clinical studies, which revealed the 5mg dosage of linagliptin was "the most suitable dose to put forward and can be considered as the therapeutic dose." (Tr. 76:21-25; 77:11-21 (Mark)). Based on the results of the clinical studies, Boehringer submitted a New Drug Application, seeking approval for linagliptin for treating type 2 diabetes at a 5mg dose. (*Id.*).

b. The '541 Patent

The '541 patent titled titled "8-[3-amino-piperidin-1-yl]-xanthines, the Preparation thereof and their Use as Pharmaceutical Compositions" was issued on May 15, 2012, and was filed as U.S. Patent No. 12/143,128 on June 20, 2008. (Stip. Facts, ECF No. 539-1, at ¶ 128). The '541 patent is a continuation of U.S. Application No. 10/639,036 (now the '955 patent), which was filed on August 12, 2003, and claims priority to U.S. Provisional Application Nos. 60/409,312 (filed on September 9, 2002), No. 60/461,752 (filed on April 10, 2003), German application nos. DE 102 38 243.3 (filed August 21, 2002), and DE 103 12 353.9 (filed March 20, 2003). (*Id.*) The '541 patent expires on August 12, 2024. (*Id.* at ¶ 115). Boehringer is listed on the face of the '541 patent as the assignee. (*Id.* at ¶ 117).

At issue in the present litigation are Patent Reference Claims 44 and 45 of the '541 patent. Claim 44 of the '541 recites: "A pharmaceutical composition comprising 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine [hereinafter "linagliptin"] and metformin." (*Id.* at ¶ 126). Claim 45 of the '541 patent recites: "A method of

treating type II diabetes mellitus comprising administering to a patient in need thereof a pharmaceutically effective amount of [linagliptin] and metformin." (*Id.* at ¶ 127).

c. The Asserted Patents

i. The '927Patent

The '927 patent, titled "Uses of DPP-IV Inhibitors," was issued on March 18, 2014, from Application No. 12/946,193 ("the '193 application"), which was filed on November 15, 2010. (*Id.* at ¶ 128). The '193 application is a continuation of U.S. Application No. 11/744,703 ("the '703 application"), filed May 4, 2007 (now U.S. Patent No. 8,232,281). (*Id.*) The '703 application claims priority to European Patent Application No. EP 06009203 (filed May 4, 2006). (*Id.*) The '927 patent expires on May 4, 2027. (*Id.* at ¶ 129). Boehringer is listed on face of the '927 patent as the assignee. (*Id.* at ¶ 131). Boehringer claims Defendants have infringed claims 7, 9, 15, 17, 19, 25 and 26 of the '927 patent.

The '927 patent describes "the use of selected DPP-IV inhibitors for the treatment of physiological functional disorders and for reducing the risk of the occurrence of such functional disorders in at-risk patient groups. In addition, the use of above-mentioned DPP-IV inhibitors in conjunction with other active substances is described, by means of which improved treatment outcomes can be achieved." (JTX-1.2).

Claim 7 of the '927 patent recites: "The method according to claim 1, wherein [linagliptin] is administered in an oral dosage of 2.5 mg or 5 mg." (*Id.* at ¶ 132).

Claim 9 of the '927 patent recites: "The method according to claim 1, wherein [linagliptin] is administered in an oral daily dose of 5 mg." (*Id.* at ¶ 133).

Claim 15 of the '927 patent recites: "The method according to claim 10, wherein [linagliptin] is administered in an oral dosage of 2.5 mg or 5 mg." (*Id.* at ¶ 134).

Claim 17 of the '927 patent recites: "The method according to claim 1O, wherein [linagliptin] is administered in an oral daily dose of 5 mg." (*Id.* at ¶ 135).

Claim 19 of the '927 patent recites: "A method of treating type II diabetes mellitus comprising administering to a patient in need thereof a pharmaceutically effective oral amount of [linagliptin] which is an oral daily dose of 5 mg, and a pharmaceutically effective amount of metformin." (*Id.* at ¶ 136).

Claim 25 of the '927 patent recites: "The method according to claim 2O, wherein th[linagliptin] is administered in an oral dosage of 2.5 mg or 5 mg." (*Id.* at ¶ 136).

Claim 26 of the '927 patent recites: "The method according to claim 20, wherein the [linagliptin] is administered in an oral daily dose of 5 mg." (*Id.* at ¶ 138).

ii. The '859 Patent

Patent '859, titled "Uses of DPP IV Inhibitors," was issued on November 3, 2015. (*Id.* at ¶ 141). The '859 patent results from U.S. Patent Application No. 14/161,007 ("the '007 application"), which was published as U.S. Patent Application Publication No. 2014/0135348 A1 ("the '348 Publication") on May 15, 2014. (*Id.*) The '007 application was filed on January 22, 2014, and is a continuation of U.S. Patent Application No. 12/946,193, filed on November 15, 2010, now the '927, which is a continuation of U.S. Patent Application No. 11/744,703 ("the '703 application"), filed on May 4, 2007, now U.S. Patent No. 8,232,281. (*Id.*) The '703 application claims priority to European Patent Application No. EP 06009203, filed May 4, 2006. (*Id.*) The '859patent expires on May 4, 2027. (*Id.*) Boehringer is listed on face of the '859 patent as the assignee. (*Id.* at ¶ 144). Boehringer claims Defendants have infringed claims 1, 14, 15, 20, and 21 of the '859 patent.

The '859 patent describes "the use of selected DPP-IV inhibitors for the treatment of physiological functional disorders and for reducing the risk of the occurrence of such functional disorders in at-risk patient groups. In addition, the use of above-mentioned DPP-IV inhibitors in conjunction with other active substances is described, by means of which improved treatment outcomes can be achieved." (JTX-2.13).

Claim 1 of the '859 patent recites:

> A method of treating type 2 diabetes comprising administering to a patient in need thereof (a) [linagliptin], or a therapeutically active salt thereof, in an oral dosage of 2.5 mg or 5 mg, and (b) metformin wherein the dose of metformin is 100 mg to 500 mg or 200 mg to 850 mg (1-3 times a day), or 300 mg to 1000 mg once or twice a day, or as delayed-release metformin in a dose of 500 mg to 1000 mg once or twice a day, or 500 mg to 2000 mg once a day, or wherein the dose of metformin is 500 mg, 850 mg or 1000 mg as a single dose with a total daily dose of metformin of 500-2850 mg, or 500 mg, 1000 mg, 1500 mg or 2000 mg metformin in delayed release form, or wherein the dose of metformin is 500 mg to 1000 mg.

(*Id.* at ¶ 145).

Claim 14 of the '859 patent recites: "An oral tablet formulation comprising [linagliptin] in an amount of 2.5 mg or 5 mg optionally in combination with metformin, and a pharmaceutically acceptable carrier or diluent." (*Id.* at ¶ 146).

Claim 15 of the '859 patent recites: "The oral tablet according to claim 14, containing 500 mg to 1000 mg metformin." (*Id.* at ¶ 147).

Claim 20 of the '859 patent recites: "A method of treating type 2 diabetes comprising administering to a patient in need thereof the oral tablet of claim 14, wherein the daily oral amount of [linagliptin] administered to said patient is 5mg." (*Id.* at ¶ 148).

Claim 21 of the '859 patent recites: "The method according to claim 5, wherein [linagliptin] in a dosage of 2.5 mg is administered twice daily." (*Id.* at ¶ 149).

C. The Specific Allegations

The parties have previously stipulated that Mylan's submission of ANDA No. 208431 infringed claims 14 and 20 of the '859 patent pursuant to 35 U.S.C. § 271(e)(2)(A). Boehringer further contends that the submission of Mylan's ANDA No. 208430 to market a generic version of Jentadueto® infringed the asserted claims of the '927 and '859 patent, specifically infringing upon claims 7, 9, 15, 17, 19, 25, and 26 of the '927 patent and claims 1, 14, 15, 20, and 21 of the '859 Patent. Boehringer also contends that the submission of Mylan's ANDA No. 208431 to market a generic version of Tradjenta®, a linagliptin product with standard doses of metformin, infringed the asserted claims of the '927 and '859 patent. Specifically, Boehringer argues that Mylan infringed upon claims 7, 9, 15, 17, 19, 25, and 26 of the '927 patent, and claim 1 of the '859 patent. Additionally, Boehringer argues that Mylan's proposed labels, described in ANDA No. 208431, promote, recommend, and encourage the administration of standard commercial doses of metformin with a 5mg oral dose of linagliptin to treat patients with type 2 diabetes. Boehringer contends that, pursuant to 35 U.S.C. § 271(b), this proposed label induces infringement of claims 7, 9, 15, 17, 19, 25, and 26 of the '927 patent and claim 1 of the '859 patent, and will induce physicians to administer the Claimed Combination Therapy.

Regarding Aurobindo, the parties have previously stipulated that Aurobindo's submission of ANDA No. 208415 infringed claims 14 and 20 of the '859 patent. Boehringer further argues the administration of linagliptin with the standard commercial doses of metformin, described in ANDA No. 208415, infringed upon claim 1 of the '859 patent. Additionally, Boehringer argues that Aurobindo's proposed labels, described in ANDA No. 208415, promote, recommend and encourage the administration of standard commercial doses of metformin with a 5mg oral dose of linagliptin to treat patients with type 2 diabetes. Boehringer contends that this proposed label

induces infringement of claim 1 of the '859 patent, and will induce physicians to administer the Claimed Combination Therapy.

In response, Defendants argue that the asserted claims are invalid for obviousness-type double patenting. Defendants contend that '859 and '927 patents were an attempt to perpetuate Boehringer's monopoly over Tradjenta and Jenataduetо beyond the expiration of the early expiring '955, '648, and '541 patents. Defendants also argue that the asserted claims are additionally invalid because they are obvious, as prior art disclosed these claims. In furtherance of this argument, Defendants posit that there are no secondary considerations that support a finding of non obviousness. Finally, Defendants argue that claims 14 and 20 of the '859 patent are invalid as anticipated.

II

A. Discussion and Conclusions of Law

1. The Asserted Claims are Invalid for obviousness-type double patenting and obviousness.

A patent is valid upon issuance. *See* 35 U.S.C. § 282(a). Each of the patents' claims are presumed valid independent of the validity of other claims. *See Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 446 (Fed. Cir. 1986) (citing 35 U.S.C. § 282). Accordingly, "the patent challenger bears the burden of proving the factual elements of invalidity [of each claim] by clear and convincing evidence . . . The trial court has the responsibility to determine whether the challenger has met its burden by clear and convincing evidence by considering the totality of the evidence, including any rebuttal evidence presented by the patentee." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1359-60 (Fed. Cir. 2007); *see also Microsoft Corp. v. i4i Ltd. P'ship, et al.*, 564 U.S. 91, 131 (2011).

Patent invalidity is an affirmative defense that "can preclude enforcement of a patent against otherwise infringing conduct." *Commil USA, LLC v. Cisco Systems, Inc.*, 135 S. Ct. 1920, 1929 (2015) (quoting 6A Chisum on Patents § 19.01, p. 19-5 (2015)); *see also* 35 U.S.C. § 282(b)(2). Defendants' invalidity defenses must each be proven by clear and convincing evidence. *Microsoft Corp.*, 564 U.S. at 95; *see also Insite Vision Inc. v. Sandoz, Inc.*, 783 F.3d 853, 858 (Fed. Cir. 2015) (quoting *Takeda Pharm. Co. v. Zydus Pharm. USA, Inc.*, 743 F.3d 1359, 1366 (Fed. Cir. 2014)). "Clear and convincing evidence has been described as evidence which proves in the mind of the trier of fact 'an abiding conviction that the truth of the factual contentions [is] highly probable.'" *Intel Corp. v. Int'l Trade Comm'n*, 946 F.2d 821, 830 (Fed. Cir. 1991) (quotation omitted).

a. The Asserted Claims are invalid for Obviousness-type double patenting.

Obviousness-type double patenting is a "judicially created doctrine that prevents a later patent from covering a slight variation of an earlier patented invention." *Sun Pharm. Indus. v. Eli Lilly & Co.*, 611 F.3d 1381, 1384 (Fed. Cir. 2010). The doctrine of double patenting "is based on the core principle that, in exchange for a patent, an inventor must fully disclose his invention and promise to permit free use of it at the end of his patent term." *Gilead Scis., Inc. v. Natco Pharma Ltd.*, 753 F.3d 1208, 1212 (Fed. Cir. 2014). This doctrine "is intended to prevent a patentee from obtaining a timewise extension of [a] patent for the same invention or an obvious modification thereof." *Sun Pharm. Indus.*, 611 F.3d at 1384 (quoting *In re Basell Poliolefine Italia S.P.A.*, 547 F.3d 1371, 1375 (Fed. Cir. 2008)). "The obviousness-type double patenting doctrine preserves 'the public's right to use not only the exact invention claimed by an inventor when his patent expires, but also obvious modifications of that invention that are not patentably distinct improvements." *Gilead Sciences, Inc.*, 753 F. 3d at 1212 . This doctrine recognizes that, "[i]f an

inventor could obtain several sequential patents on the same invention, he could retain for himself the exclusive right to exclude or control the public's right to use the patented invention far beyond the term awarded to him under the patent laws." *Id.*

Analyzing claims for obviousness-type double patenting requires comparing "claims in an earlier patent to claims in a later patent or application." *Geneva Pharm., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1377 n.1 (Fed. Cir. 2003). Thus, the starting point in such an analysis is the reference claims of the earlier patent. This requires a two-step analysis, first "the court 'construes the claim[s] in the earlier patent and the claim[s] in the later patent and determines the differences.' Second, the court 'determines whether those differences render the claims patentably distinct.'" *Sun Pharm. Indus.*, 611 F.3d at 1385 (quoting *Pfizer, Inc. v. Teva Pharm. USA, Inc.*, 518 F.3d 1353, 1363 (Fed. Cir. 2008)). "A later claim that is not patentably distinct from, i.e., is 'obvious over or anticipated by,' an earlier claim is invalid for obviousness-type double patenting." *Sun Pharm. Indus.*, 611 F.3d at 1385 (quoting *Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 968 (Fed. Cir. 2001)).

Step two of the obvious-type double patenting "is analogous to an obviousness analysis under 35 U.S.C. § 103." *Abbvie Inc. v. Mathilda & Terence Kennedy Inst. of Rheumatology Tr.*, 764 F.3d 1366, 1378 (Fed. Cir. 2014) (quoting *Amgen Inc. v. F. Hoffman-LaRoche Ltd*, 580 F.3d 1340, 1361 (Fed. Cir. 2009)). "The law of obviousness-type double patenting looks to the law of obviousness generally." *Id.* "Thus, if the later expiring patent is merely an obvious variation of an invention disclosed and claimed in the [reference] patent, the later expiring patent is invalid for obviousness-type double patenting." *Abbvie Inc.*, 764 F.3d at 1379 (quotations omitted). Like an analysis under § 103, analysis under obvious-type double patenting "entails determining . . . whether one of ordinary skill in the art would have had reason or motivation to modify the earlier

claimed compound to make the compound of the asserted claim with a reasonable expectation of success." *Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1298 (Fed. Cir. 2012).

Finally, "the focus of the [ODP] doctrine [] rests on preventing a patentee from claiming an obvious variant of what it has previously claimed, not what it has previously disclosed." *Bayer Pharma AG v. Watson Labs., Inc.*, 212 F. Supp. 3d 489, 513 (D. Del. 2016) (quoting *Eli Lilly & Co. v. Teva Parenteral Med., Inc.*, 689 F.3d 1368, 1377 (Fed. Cir. 2012)) *see also Ortho Pharma. Corp. v. Smith*, 959 F.2d 936, 943 (Fed. Cir. 1992) ("It is the claims, not the specification, that define an invention . . . . And it is the claims that are compared when assessing double patenting.").

i. Step One: Comparison between the Claims

Boehringer's '541 patent expires on August 12, 2023, and claims a method of treating type 2 diabetes with a "pharmaceutically effective amount" of linagliptin and metformin, as well as a pharmaceutical composition containing linagliptin and metformin. (D FF 411-414). In contrast, the Asserted Patents expire on May 4, 2027, almost four years later, and claim compositions and methods of treating type 2 diabetes with 2.5 or 5 mg of linagliptin and standard doses of metformin, or no metformin at all. (Defs. PFoF at ¶¶ 135; 139–146; 150;153–158; 412; 415). The following chart is illustrative of the differences between the '541 reference claims and the asserted claims:

Reference Claim	**Asserted Claims**
'541 patent, Claim 44 (Tablet claims) A pharmaceutical composition comprising [linagliptin] and metformin.	**'859 patent, Claim 14** An oral tablet formulation comprising [linagliptin] in an amount of 2.5 mg or 5 mg optionally in combination with metformin, and a pharmaceutically acceptable carrier or diluent.

	'859 Patent, Claim 15 The oral tablet according to claim 14, containing 500 mg to 1000 mg metformin.
'541 patent, Claim 45 (Method claim) A method of treating type II diabetes mellitus comprising administering to a patient in need thereof a pharmaceutically effective amount of [linagliptin] and metformin.	**'859 patent, Claim 1** A method of treating type 2 diabetes comprising administering to a patient in need thereof [linagliptin], or a therapeutically active salt thereof, in an oral dosage of 2.5 mg or 5 mg, and (b) metformin wherein the dose of metformin is 100 mg to 500 mg or 200 mg to 850 mg (1-3 times a day), or 300 mg to 1000 mg once or twice a day, or as delayed-release metformin in a dose of 500 mg to 1000 mg once or twice a day, or 500 mg to 2000 mg once a day, or wherein the dose of metformin is 500 mg, 850 mg or 1000 mg as a single dose with a total daily dose of metformin of 500-2850 mg, or 500 mg, 1000 mg, 1500 mg or 2000 mg metformin in delayed release form, or wherein the dose of metformin is 500 mg to 1000 mg.
	'859 patent, Claim 20 A method of treating type 2 diabetes comprising administering to a patient in need thereof the oral tablet of claim 14, wherein the daily oral amount of [linagliptin] administered to said patient is 5mg.
	'859 patent, Claim 21 The method according to claim 5, wherein [linagliptin] a dosage of 2.5 mg is administered twice daily.

	Claim 5: A method according to claim 2, wherein the dosage of [linagliptin] is 2.5 mg. Claim 2: A method according to claim 1 (see above) wherein [linagliptin] and metformin are administered orally in the form of a fixed combination.
	'927 patent, Claim 7 The method according to claim 1, wherein [linagliptin] is administered in an oral dosage of 2.5 mg or 5 mg. Claim 1: A method of treating type-II diabetes . . . administering to a patient in need thereof a pharmaceutically effective amount of metformin, which is from 300mg to 1000mg once or twice a day, or a delayed release metformin in a dose of 500mg to 1000mgnce a day.
	'927 patent, Claim 9 The method according to claim 1 [(see above)], wherein [linagliptin] is administered in an oral daily dose of 5 mg.
	'927 patent, Claim 15 The method according to claim 10, wherein [linagliptin] is administered in an oral dosage of 2.5 mg or 5 mg. Claim 10: A method of treating type 2 diabetes or pre-diabetes compricing administering to a patient in need thereof a therapeutically effective oral dose of [linagliptin] in combination with a therapeutically effective dose of metforminm, which is 500mg, 850mg or 1000mg metformin as a single dose with a total daily dose of metformin of 500-2850mg, or which is 500 meg, 1000mg, 1500mg or 2000mg metformin in delayed release form.

	'927 patent, Claim 17 The method according to claim 10 [(see above)], wherein [linagliptin] is administered in an oral daily dose of 5 mg.
	'927 patent, Claim 19 A method of treating type II diabetes mellitus comprising administering to a patient in need thereof a pharmaceutically effective oral amount [linagliptin] which is an oral daily dose of 5 mg, and a pharmaceutically effective amount of metformin.
	'927 patent, Claim 25 The method according to claim 20, wherein [linagliptin] is administered in an oral dosage of 2.5 mg or 5 mg. Claim 20: A method of treating type 2 diabetes or pre-diabetes comprising administering to a patient in need thereof a therapeutically effective oral dose of [linagliptin] in combination with a therapeutically effective dose of metformin . . . .
	'927 Patent, Claim 26 The method according to claim 20 [(see above)], wherein [linagliptin] is administered in an oral daily dose of 5 mg.

Upon comparison, this court recognizes two differences between the reference claims and the asserted claims. First, the reference claims recite the use of linagliptin and metformin in "pharmaceutically effective amounts." In contrast, the asserted claims specify doses for both linagliptin and metformin. Additionally, as to the method of administering the drugs, the reference

claims do not specify how the drugs are intended to be administered. In contrast, the asserted claims specify that the drugs are to be administered orally. Moreover, asserted '859 claims 14 and 15 specify that the drugs should be taken via an oral tablet. Apart from the dosages of both linagliptin and metformin, and the oral administration of the drugs, there are no differences between the reference claims and the asserted claims. This court will next determine whether these two differences are patentably distinct.

ii. Step Two: Determine Whether the Claims are Patentably Distinct

Here, Defendants bear the burden of proving by clear and convincing evidence that the asserted claims of the '859 and '927 patents are invalid. The scope and analysis of the patents-in-suit is to be undertaken by the hypothetical "person of ordinary skill in the art" or "skilled artisan." The Court finds, as the parties more or less agree, that at the time of the patents-in-suit, a person of ordinary skill in the art relating to the inventions claimed by both the '859 and '927 patent would

> have an advanced degree in the pertinent field, such as pharmacology, pharmaceutics, medicinal chemistry, clinical research science, and medicine. To the extent a person does not have the necessary expertise in all the disciplines, he or she would work with another person or a team of persons, with the necessary experience and expertise.
>
> (Def. PFoF ECF No. 597 at ¶ 314).

Defendants advance the position that the reference claims and the prior art disclose the asserted claims, specifically: (1) the use of linagliptin; (2) to treat type 2 diabetes; (3) in dosages of 2.5 or 5 mg; (4) combined with metformin; (5) in "pharmaceutically" or "therapeutically effective" amounts of metformin, or in dosages ranging from 100–2850 mg; (6) through oral administration or in oral tablets. Thus, any differences between the asserted claims and the reference claims are not patentably distinct.

1. Linagliptin Dosages

Defendants argue that the asserted claim's linagliptin dosages are not patentably distinct in light of prior art, specifically U.S. Patent Publication No. 2004/0097510 ("the '510 publication"), which was published in 2004. (*See* JTX-011). The '510 publication is the published application that issued Boehringer's '955 Patent and is cited on the face of both the '927 and '859 patents. (Pl's. PFoF at ¶ 330; Defs. PFof at ¶315). The "field of invention" of the '510 publication "relates to compounds having valuable pharmacological properties, particularly in inhibiting [the] effect on the activity of the enzyme [DPP-IV]," and the "present invention" "relates to a new substituted xanthines of general formula." (JTX-11.0002). The '510 publication discloses approximately 7,000 DPP-IV inhibitors, and it also discloses a list of the thirty "most particularly preferred" DPP-IV inhibitors.

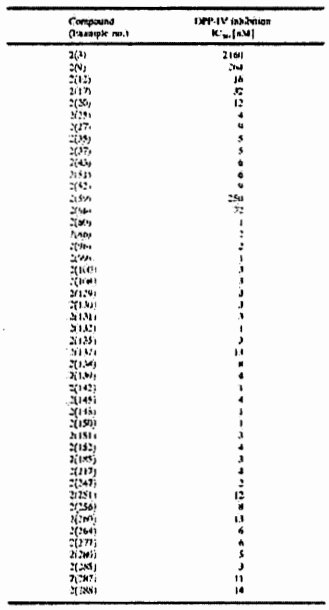
It is important to note that the reference claims themselves recite linagliptin. Thus, determining why a POSA would select linagliptin is irrelevant to the obviousness-type double patenting analysis. However, for the sake of completeness, the use of linagliptin is disclosed by the '510 prior art in several places. First, linagliptin is listed in paragraph 2400, which provides the chemical name for linagliptin. (*See* JTX 11.0057 at ¶ 2400).

> **[2400]** (142) 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)amino-piperidin-1-yl)-xanthine

Second, the '510 publication lists linagliptin as one of the thirty "[m]ost particularly preferred" DPP-IV inhibitors. (JTX-11.0009, at ¶¶ 232, 245).

> **[0232]** Most particularly preferred are the following compounds of general formula I:
>
> **[0245]** (13) 1-[(4-methyl-quinazolin-2-yl)methyl]-3-methyl-7-(2-butyn-1-yl)-8-(3-(R)-amino-piperidin-1-yl)-xanthine,

Third, paragraph 245 of the '510 publication lists linagliptin as compound 2(142), having an IC_{50} value of 1nM. (JTX-11.0013).[4]



This list shows linagliptin, with an IC_{50} value of 1nM, as one of the most potent DPP-IV inhibitors listed. Dr. Grass explained, "Linagliptin has an IC_{50} value of 1 nanomolar. And 1 nanomolar is the lowest value that's found on this table. So the lowest value would represent the highest potent." (Tr. 734:5–7 (Grass)).

Boehringer argues that a POSA would not be motivated to select linagliptin from the approximately 7,000 compounds disclosed in the '510 publication. However, of the approximately 7,000 compounds disclosed, the '510 publication specifies thirty of the "most particularly preferred" DPP-IV inhibitors. Further, the '510 publication lists linagliptin as one of the most

[4] Linagliptin is listed as compound 2(142) with a 1nM IC_{50} value. An IC_{50} value is "a concentration which inhibits the enzymatic activity of DPP-IV by 50%, in a test tube under special conditions." (Tr. 49:18 to 50:4 (Mark)).

potent DPP-IV inhibitors with a IC_{50} value of 1nM, thus making it highly potent. Though Boehringer contends that a POSA would not be motivated to choose linagliptin from this list, as there were other DPP-IV inhibitors that are similarly highly potent, linagliptin was tied with only five other DPP-IV inhibitors. Thus, out of the approximately 7,000 DPP-IV inhibitors the '510 publication disclosed, the '510 publication discloses linagliptin as one of the "most particularly preferred" and as one of the most potent. Accordingly, it is likely that with linagliptin's high potency, and designation as one of the "most particularly preferred," a POSA would have been motivated to select linagliptin.

However, the '510 publication discloses a preferred dosage range, which applies to all compounds disclosed in the publication, in a 1-1000mg dosage range, preferably 1-100mg, taken one to four times a day. (JTX-11.0013).

> **[0300]** The dosage required to achieve such an effect is expediently, by intravenous route, 1 to 100 mg, preferably 1 to 30 mg, and by oral route 1 to 1000 mg, preferably 1 to 100 mg, in each case 1 to 4 times a day. For this purpose, the compounds of formula I prepared according to the invention, optionally combined with other active substances, may be incorporated together with one or more inert conventional carriers and/or diluents, e.g. with corn starch, lactose, glucose, microcrystalline cellulose, magnesium stearate, polyvinylpyrrolidone, citric acid, tartaric acid, water, water/ethanol, water/glycerol, water/sorbitol, water/polyethylene glycol, propylene glycol, cetylstearyl alcohol, carboxymethylcellulose or fatty substances such as hard fat or suitable mixtures thereof into conventional galenic preparations such as plain or coated tablets, capsules, powders, suspensions or suppositories.

When asked if a POSA would understand the dosage range to be between 1 and 400 mg, Dr. Accili explained that to determine the dosage between 100 and 400 milligrams, and to determine the amount of times the linagliptin is taken per day, leaves an infinite number of possibilities. (Tr. 546:18-23 (Accili)). But, because Dr. Accili explained a once daily dosage was deemed preferable and would be commercially successful, that would limit the range. (Tr. 523:9-10; 556:25 to 57:3 (Accili)). Further, Defendants' experts testified that a preferred once-daily dosage 1-100mg was sufficiently narrow for a POSA to consider a dosage from 2.5 mg to 5mg of

linagliptin. For example, Dr. Grass testified that this narrow 1-100mg range "is a dose range that can be addressed in a typical dose-ranging study." (Tr. 736:1-4 (Grass)). Plaintiffs' expert Dr. Lam also conceded a higher dose range of 2.5 to 600mg of linagliptin was not broad. (Tr. 1044:7-22 (Lam)). Accordingly, Dr. Accili limited the range to 1 to 100mg. (Tr. 523:5-13 (Accili)).

Here, the dispute is whether there was motivation for a POSA to select the claimed dosages of linagliptin from the range disclosed in the prior art. *See Galderma Labs., L.P.*, 737 F.3d at 737. "Ordinarily, 'where there is a range disclosed in the prior art, and the claimed invention falls within that range, there is a presumption of obviousness.'" *Tyco Healthcare Grp. LP v. Mut. Pharm. Co., Inc.*, 642 F.3d 1370, 1372–73 (Fed. Cir. 2011) (quoting *Iron Grip Barbell Co.*, 392 F.3d at 1322). "In these circumstances, . . . the burden of production falls upon the patentee to come forward with evidence that (1) the prior art taught away from the claimed invention; (2) there were new and unexpected results relative to the prior art; or (3) there are other pertinent secondary considerations." *Galderma Labs., L.P*, 737 F.3d at 737-38 (citing *Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd.*, 719 F.3d 1346, 1352-54 (Fed. Cir. 2013)).

"Where the difference between the claimed invention and the prior art is some range or other variable within the claims, the patentee must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results." *Warner Chilcott Co., LLC v. Teva Pharm. USA*, Inc., 89 F. Supp. 3d 641, 673 (D.N.J. 2015) (quoting *Iron Grip Barbell Co., Inc. v. USA Sports, Inc.*, 392 F.3d 1317, 1322 (Fed. Cir. 2004)). However, "where selection of the claimed amount within the prior art range results in 'only a difference in degree from the prior art results,' the claimed amount is not critical." *Id.* (quoting *Galderma Labs., L.P.*, 737 F.3d at 737-39). Courts confronted with similar ranges like the range found in the '510 publication have found claims falling within disclosed range obvious in light of prior art. For example, in

Warner Chilcott Co., LLC, the court determined that a claim of 100mg was obvious when considering the prior arts range of 75 mg to 250mg. 89 F.Supp.3d at 656. Similarly, in *Galderma Labs., L.P.*, the Federal Circuit concluded that a claim of 0.3% adapalene was obvious over a 100-fold prior art range (0.01–1%)—the same size range as here. 737 F.3d 731, 738 (Fed. Cir. 2013).

A POSA would be familiar with routine dose-ranging studies, as experts at trial testified that dose-ranging studies were included in general guidelines for FDA approval. ((Tr. 1356:7-10 (Accili); Tr. 1060:2-5 (Lam)). For example, the O'Grady reference, which was published in 1990, provides an example of "simple rising dose design," where dosages are given sequentially from a low dose to a high dose. (Def. PFoF, ECF No. 597 at ¶ 341). At trial, Dr. Grass explained that dose ranging studies are "conducted starting with a low dose, and sequentially moving through increasing doses," "proceed[ing] with the initial dose and then doubl[ing] and quadrupl[ing]" one dose at a time to evaluate "whether or not there are any limiting side effects" up to "until the highest dose unless the trial is terminated because there was some limiting toxicity." (Tr. 720:6 to 721:10 (Grass)). Dr. Grass testified that a real world example of a dose ranging study could be found in the Bergman reference, a prior art published in 2006 in the Journal of Clinical Therapeutics, where a study was conducted using sitagliptin. (Tr. 721:15 to 24 (Grass)). There, the initial dose level was 25 mg, and then the range was increased to 50mg, then 100mg, then 200mg, and finally 400mg. (Tr. 722:18- 22) (Grass)). In another dose-ranging study example, the Bachovchin patent application, described a dose ranging study for a DPP-IV inhibitor, where "the dosage should be increased by smaller increments until the optimum effect under the circumstances is reached; for convenience the total daily dose and may be divide and administered in portions during the day if desire . . . [b]asically describing giving a . . . lower dose, and then increasing the dose until you

achieve an optimum effect. (Tr. 725:18 to 726:6 (Grass)).[5] Thus, in order to optimize drug dosages, experts testified that a POSA would conduct a dose ranging study. (Tr. 956:18-20 (Lenhard)).

Boehringer argues that, if conducing a dose ranging study, a POSA would be motivated by the '510 publication to begin the study at 75mg, and thus would never arrive at the claimed 2.5mg and 5mg dosages of linagliptin. Boehringer cites to specific examples found in the '510 publication that include specific dosages on oral tablets for the disclosed DPP-IV inhibitors, specifically, Example 4 of the '510 publication describes "[c]oated tablets containing 75 mg of active substance," along with other components of the tablets, including the amount, size, and shape. (Pl's. PFoF at ¶ 349; JTX-11.67).

EXAMPLE 4

Coated tablets containing 75 mg of active substance

1 tablet core contains:

active substance	75.0 mg
calcium phosphate	93.0 mg
corn starch	35.5 mg
polyvinylpyrrolidone	10.0 mg
hydroxypropylmethylcellulose	15.0 mg
magnesium stearate	1.5 mg
	230.0 mg

[2899] Preparation:

[2900] The active substance is mixed with calcium phosphate, corn starch, polyvinylpyrrolidone, hydroxypropylmethylcellulose and half the specified amount of magnesium stearate. Blanks 13 mm in diameter are produced in a tablet-making machine and these are then rubbed through a screen with a mesh size of 1.5 mm using a suitable machine and mixed with the rest of the magnesium stearate. This granulate is compressed in a tablet-making machine to form tablets of the desired shape.

[2901] Weight of core: 230 mg

[2902] die: 9 mm, convex

[2903] The tablet cores thus produced are coated with a film consisting essentially of hydroxypropylmethylcellulose. The finished film-coated tablets are polished with beeswax.

[2904] Weight of coated tablet: 245 mg.

[5] U.S. Publication No. 2003/0153509 ("Bachovchin") was published on August 14 2003. *See* JTX-16; Pls. PFoF at ¶ 383.

Example 5 describes "[t]ablets containing 100mg of active substance," in addition to the amount, size, and shape of the tablet.

EXAMPLE 5

Tablets containing 100 mg of active substance

Composition:
1 tablet contains:

active substance	100.0 mg
lactose	80.0 mg
corn starch	34.0 mg
polyvinylpyrrolidone	4.0 mg
magnesium stearate	2.0 mg
	220.0 mg

[2905] Method of Preparation:

[2906] The active substance, lactose and starch are mixed together and uniformly moistened with an aqueous solution of the polyvinylpyrrolidone. After the moist composition has been screened (2.0 mm mesh size) and dried in a rack-type drier at 50° C. it is screened again (1.5 mm mesh size) and the lubricant is added. The finished mixture is compressed to form tablets.

[2907] Weight of tablet: 220 mg

[2908] Diameter: 10 mm, biplanar, facetted on both sides and notched on one side.

(Pls. PFoF at ¶ 350; JTX-11.67)

Finally, Example 7 describes "[h]ard gelatin capsules containing 150 mg of active substance," and also describes the amount, size, and shape of the capsule.

EXAMPLE 7

Hard gelatine capsules containing 150 mg of active substance

1 capsule contains:

active substance	150.0 mg
corn starch (dried	approx. 80.0 mg
lactose (powdered)	approx. 87.0 mg
magnesium stearate	3.0 mg
	approx. 420.0 mg

[2912] Preparation:

[2913] The active substance is mixed with the excipients, passed through a screen with a mesh size of 0.75 mm and homogeneously mixed using a suitable apparatus. The finished mixture is packed into size 1 hard gelatine capsules.

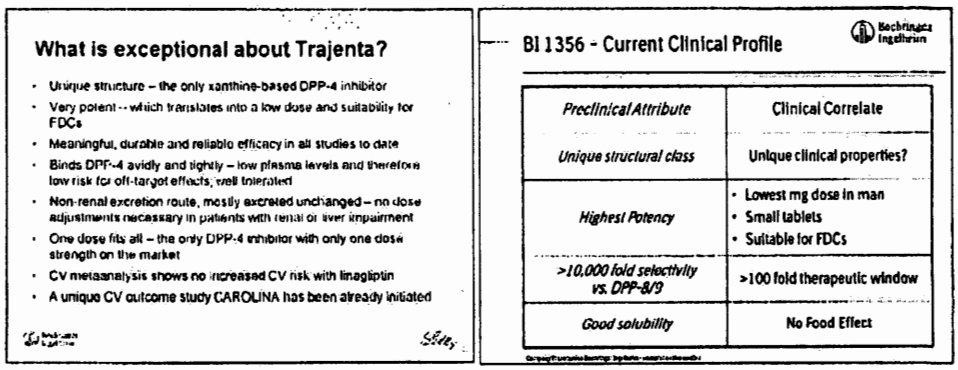
[2914] Capsule filling: approx. 320 mg

[2915] Capsule shell: size 1 hard gelatine capsule.

Examples and disclosures must be read in context of the patent or publication as a whole, and courts urge against taking statements out of context. *Panduit Corp. v. Dennison Mfg. Co.*, 810

F.2d 1561, 1578 (Fed. Cir. 1987); *see also Bausch & Lomb, Inc.*, 796 F.2d at 448. "It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art." *Id.*

Here, it is important to note that there is a correlation between potency and dosage. (Def. PFoF, ECF No. 597 at ¶553). Increasing the dose of a drug increases the rate at which the drug is then excreted through the kidney. (Tr. 1347:9-11 (Accili)). Obviously, when a substance has a higher potency effect on the body, the use of a lesser amount of that substance will have a therapeutic effect. Accordingly, the use of a lesser amount of linagliptin will have a therapeutic effect on the body. Thus, a therapeutic dose of linagliptin is less than other DPP-IV inhibitors. Although Boehringer argues otherwise, it identified that because linagliptin is highly potent, it would result in a low dosage. (Tr. 1464:23 to 1467:14). So would a POSA.



What is exceptional about Trajenta?

- Unique structure – the only xanthine-based DPP-4 inhibitor
- Very potent -- which translates into a low dose and suitability for FDCs
- Meaningful, durable and reliable efficacy in all studies to date
- Binds DPP-4 avidly and tightly – low plasma levels and therefore low risk for off-target effects; well tolerated
- Non-renal excretion route, mostly excreted unchanged – no dose adjustments necessary in patients with renal or liver impairment
- One dose fits all – the only DPP-4 inhibitor with only one dose strength on the market
- CV metaanalysis shows no increased CV risk with linagliptin
- A unique CV outcome study CAROLINA has been already initiated

BI 1356 - Current Clinical Profile

Boehringer Ingelheim

Preclinical Attribute	Clinical Correlate
Unique structural class	Unique clinical properties?
Highest Potency	• Lowest mg dose in man • Small tablets • Suitable for FDCs
>10,000 fold selectivity vs. DPP-8/9	>100 fold therapeutic window
Good solubility	No Food Effect

(DTX-299_0035).

Boehringer argues that a POSA would initially chose a dose study at the 75mg range in accordance with the examples in the prior art ('510 publication), and work upwards, doubling the dosage to reach a therapeutically effective amount of linagliptin. However, this argument is backwards and does not comport with the common sense of a POSA. It discounts the high potency of linagliptin. As stated above, the higher potency effect correlates with a lower dose of a drug,

which would motivate a POSA to perform dose ranging tests at either the lower end of the disclosed dose range (1-100mg) or begin dose range tests at 75mg, but take into account linagliptin's high potency and divide the dose in some faction to find a therapeutically effective dose. Thus, taking the entirety of the '510 publication, including: (1) Examples 4 and 5, which apply to all 7000 compounds that the '510 publication discloses; (2) that the '510 publication lists linagliptin as one of the most potent DPP-IV inhibitors with a IC_{50} value of 1nM, making it highly potent; and (3) that the '510 publication discloses linagliptin as one of the "most particularly preferred" DPP-IV inhibitors; it is likely that a POSA, taking all of the above considerations into account, including the above referenced prior art, would be motivated to begin dose ranging studies on linagliptin, starting at the low end of the 1-100mg range. Even if POSA would conduct a dose ranging study starting at the 75mg dose disclosed by Example 4, a POSA would determine from the '510 publication's disclosure of the linagliptin being the most potent DPP-IV inhibitor, that an amount less than 75mg may be appropriate. Thus, a POSA, using a common sense theory, may use this same doubling formula in reverse, starting at 75mg and dividing by a half. Because there is need to limit dosage of DPP-IV inhibitors to lessen the likelihood of renal impairment, to maximize the therapeutic effect with the least amount of side effects, a POSA would be motivated to find the precise dosage of the most potent DPP-IV.

Additionally, prior art existed that disclosed different types of DPP-IV inhibitors and their dosages. For example, both vildagliptin and sitagliptin were previously disclosed in Gwaltney.[6]

[6] Gwaltney & Stafford, *Inhibitors of Dipeptidyl Peptidase 4*, Annual Reports in Medicinal Chemistry, Vol. 49: 149-165 (2005) ("Gwaltney") (JTX-013).

Later prior art disclosed the dosages for each: (1) in Brazg,[7] an abstract from a scientific meeting, the prior art discloses that sitagliptin "was administered as 50 milligrams twice a day" (i.e., "100 milligrams") when added to ongoing metformin therapy (>"1500 milligrams") (JTX-013.0001) (Tr. 751:7–11(Grass); Tr. 866:12–867:3(Lenhard)); and (2) Ahren,[8] an article, published in December 2004, that discloses vildagliptin in a dosage of 50 miligrams once a day, when added with ongoing metformin therapy. (JTX-013.0001; Tr. 751:21–752:1(Grass); Tr. 865:26–866:4(Lenhard)). Sitagliptin has a 18nM IC_{50} value, while vildagliptin has a 4nM IC_{50} value. (Defs. PFoF at ¶ 370). In summary, Dr. Grass explained that a POSA would consider this information in determining the appropriate dosage of linagliptin and that:

> one would recognize that linagliptin is disclosed in the '510; it's a compound that's shown to have the low -- the lowest IC_{50} value or the greatest potency; there's a preferred dose range of 1 to 100 milligrams; and there's a preferred list of [DPP-IV's] in which linagliptin is a member; one would be guided through that information of looking at the lowest end of the dose range for the most potent [DPP-IV]; one would be aware of the [sitagliptin and vildagliptin's potency and dosage] information . . . and the potencies and dosages here showing compounds that are less potent and higher dosages than the low end of the range; and it's not inconsistent with what the '510 discloses.

(Tr. 752:15 – 18 (Grass)).

Finally, in addition to the prior art that would motivate a POSA to conduct dose ranging studies of linagliptin starting at the low end of the 1 to 100mg range or starting at 75mg, and dividing in half to reach a therapeutically effective amount, Dr. Dugi, one of the listed inventors, testified that the FDA expects drug developers to choose the lowest effective dose for several

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[7] Brazg, et al., "Effect of Adding MK-0431 to On-Going Metformin Therapy in Type 2 Diabetic Patients Who Have Inadequate Glycemic Control on Metformin," Abstract # 11-OR,65th Scientific Sessions Diabetes Pro, American Diabetes Association, Chicago (2005) ("Brazg").

[8] Twelve- and 52-Week Efficacy of the Dipeptidyl Peptidase IV Inhibitor LAF237 in Metformin-Treated Patients With Type 2 Diabetes" by Ahren et al. ("Ahren").

reasons, including: (1) a low dose may result in a smaller, easier to swallow tablet; (2) a low dose is easier to formulate in combination pills; (3) a low dose may result a lower risk of drug to drug interactions; and (4) a low dose may reduce the risk of side effects. (Tr. 1464:11-17; 1476:4 to 1477-16 (Dugi)).

Boehringer argues that are other factors to consider that could impact the dose of a drug, and thus a POSA would not rely solely on the IC_{50} value of linagliptin, and its high potency when determining where to being dose ranging studies. Instead, to determine a human dose, a POSA would consider, along with an IC_{50} value: the rate of absorption, aqueous solubility, lipophilicity, bioavailability, AUC, Cmax, Tmax, strength of binding/Ki, dosing interval, fraction of dose that reaches the site of action, fraction of drug that enters systemic circulation unchanged, food effect, duration of action/Koff, drug metabolism (location, rate, method), first path (pass) effect, mechanisms of drug clearance, amount of drug cleared through an organ at a particular dose, elimination half-life, presence of an (active) metabolite, elimination rate constant, drug-drug interactions, toxicity, side effects, volume of distribution, and stability in the stomach/gut. (PTX-560; *see also* Tr. 566:8-14 (Accili); Tr. 760:5-9 (Grass)). However, while the IC_{50} value alone is not enough to inform a POSA what the exact dose of a compound should be, it would motivate a POSA to begin dose ranging studies based on the potency of the compound. Thus, while an IC_{50} compound is not the only factor that affects a drug dosage, it is an important factor. (Tr. 754:13-16 (Grass)).

Certainly, Boehringer recognizes the importance of the IC_{50} value and the potency of linagliptin. When Boehringer published the both the '859 and '927 patents in the Orange Book, they refereed to linagliptin's IC_{50} value. Boehringer specifically stated that "[t]hese DPP-IV inhibitors are distinguished from structurally comparably DPP-IV inhibitors, as they combine

exceptional potency and long lasting effect with favorable pharmacological properties . . . ." (JTX-1.14; JTX-2.16 (emphasis added)). Within both '859 and '927 patents, Boehringer does not reference any of the "other factors" that it now contends are equally, if not more important, than a compound's IC_{50} value and potency. Thus, it does not follow now that Boehringer diminishes the significance of linagliptin's high potency and IC_{50} value.

In summary, the reference claims disclose linagliptin, however; these claims do not disclose a dosage. Turning to the second prong of the obviousness-type double patenting test, this Court must determine if the differences between the asserted claims and the reference claims are patentably distinct. In this regard, the '510 publication discloses linagliptin in a 1-100mg range, to treat type 2 diabetes. Additionally, because the '510 publication discloses the high potency of linagliptin, a POSA would be motivated to conduct dose-ranging studies on the low end of the previously disclosed 1-100mg range, or starting at 75mg, and dividing in half backwards, to optimize the linagliptin dosages. Even more, through routine experimentation, a POSA would have a reasonable expectation of arriving at the claimed 2.5mg and 5mg dosages.

Accordingly, this Court finds that the asserted claims and the references regarding linagliptin are not patentably distinct.

2. Metformin[9]

Defendants also argue that prior art also discloses metformin dosages, thus any difference between the reference claims and the asserted claims are not patentably distinct. Defendants

[9] Defendants also claim both the '510 Publication and the Glucophage label disclose that linagliptin and metformin may be administered orally; thus any perceived difference between the reference claim and asserted claims regarding oral dosages is not patentably distinct. According to the '510 publication and the Glucophage label, linagliptin may be administered orally through tablets. (*See* JTX-11.13, ¶. 300; JTX-11.67-.68; DTX-39.1).

point to the Glucophage label, the Ahren article and the Hughes international patent application.[10] (Tr. 534:17–23 (Accili)). The Glucophage Label is a prescription label for Glucophage and Glucophage XR, that was published in 2003. (DTX-39; Tr. 500:14-15 (Accili)). These drugs contain metformin as the active ingredient. (DTX-39.1). The Glucophage and Glucophage XR label states that the Glucophage tablets contain 500mg, 850mg or 1000mg of metformin, and Glucophage XR tables contain 500mg or 750mg of metformin. (DTX-39.1). Below is a comparison of the metformin dosages claimed by the '859 and '927 patents, and the dosages found in the Glucophage label.

Glucophage Label Metformin Dosages	**Asserted Claims Metformin Dosages**
Glucophage tablet: 500mg, 850mg or 1000mg of metformin Glucophage XR tablet: 500mg or 750mg of metformin	'859 Patent, Claim 15: 500mg to 1000mg metformin '859 Patent, Claim 1: 100 mg to 500 mg or 200 mg to 850 mg (1-3 times a day), or 300 mg to 1000 mg once or twice a day, or as delayed-release metformin in a dose of 500 mg to 1000 mg once or twice a day, or 500 mg to 2000 mg once a day, or wherein the dose of metformin is 500 mg, 850 mg or 1000 mg as a single dose with a total daily dose of metformin of 500-2850 mg, or 500 mg, 1000 mg, 1500 mg or 2000 mg metformin in delayed release form, or wherein the dose of metformin is 500 mg to 1000 mg. '927 Patent, Claim 9: 300mg to 1000mg once or twice a day, or a delayed release metformin in a dose of 500mg to 1000mgnce a day. '927Patent, Claim 15: 500mg, 850mg or 1000mg metformin as a single dose with a total daily dose of metformin of 500-2850mg, or

[10] WO 2005/117861 by Thomas Hughes ("Hughes") is an international patent application published on December 15, 2005. (JTX-15.1.)

	which is 500 meg, 1000mg, 1500mg or 2000mg metformin in delayed release form.

At trial, Dr. Accili testified that prior to May 2006, a POSA would know that

> there are two formulations [of metformin], the regular formulation and the extended release formulation[:] the [regular formation comes in] three ...varieties, 500, 850 and 1000 milligrams; and it's given with low doses initially once or twice a day, gradually increasing the dose up to 2.5 grams (2550 milligrams)[; and] the XR, the extended release [form of metformin] comes in two [varieties], the 500 and the 750[mg] tablets . . . so you start once a day with the low dose, gradually move . . . up to 2000[mg] . . . given once a day[.]
>
> (Tr. 520:10-23) (Accili)).

Dr. Accili also confirmed that these the doses of metformin were being used by physicians prior to May of 2006, and that he had personally used these doses of metformin in the United States prior to May of 2006, and as early as 2003. (DTX-39.0028; Accili (Tr. 500:3-503:22; 503:6-14) (Accili); DFF387). He noted that the Glucophage label was contained in the 2003 Physician's Desk Reference book, which is a "compilation of all the prescribing information of all FDA approved drugs." (Tr. 500:24 to 501:8 (Accili); DTX-16.2-.10).

At trial, Dr. Mark confirmed that "[the] dosage strengths [] recited in claim 1" of the '927 patent are "the same dosage strengths that are also recited in the metformin label," and agreed that "the dosage strengths that are in the [Glucophage] label [] fall within [the] range that's claimed in claim 1 of the ['927] patent." (Tr. 142:23-144:10 (Mark); Def. PFoF at ¶ 386). Regarding metformin and combination therapy, Dr. Accili also explained that the Glucophage label teaches the use of metformin in combination therapy. (Tr. 503:17-22 (Accili)). Two prior arts specifically disclose metformin in combination with DPP-IV inhibitors: the Hughes patent application and the Ahren article.

The Hughes patent application was published on December 15, 2005, and states that the invention relates to "a method of treatment . . . wherein the patient is treated with a [DPP-IV inhibitor] . . . and metformin." (JTX.15.2). The Hughes patent further discloses "[i]t has now been surprisingly found that DPP-IV inhibitors . . . can be used in combination with Metformin to maintain lower blood glucose levels and/or lower [HbA1c] level . . . this invention provides a method for controlling glucose levels [and HbA1c] . . . comprising administering a therapeutically effective amount of metformin and a DPP-IV inhibitor[.]" (JTX-15.13). Finally, the Hughes patent states "satisfactory results are obtained when Metformin is administered at a daily dosage of from about 50 mg to 3000 mg, preferably from about 500 mg to about 2000 mg. Metformin can be administered . . . as 500 mg tablets." (JTX-15.23). Additionally, the Ahren article, published in December 2004, also discloses the combination of metformin and DPP-IV inhibitors to treat patients with type-2 diabetes, and discusses the results of a study that tested vildagliptin in combination with metformin. (Tr. 512:20-513:12) (Accili)). There, the article discloses metformin doses of 1,500mg-3,000mg per day, in combination with another DPP-IV inhibitor. (JTX-12.1; Tr. 535:2-4 (Accili)).

Based on the above, it is clear that metformin and its dosages are disclosed in prior art. In summary, by 1995, metformin "was approved for use or sale in the United States[,] and clinically the combination of metformin and sulfonylurea was shown to be safe and effective." (Tr. 519:15-18) (Accili)). Prior art also discloses the combination of metformin and DPP-IV inhibitors, as in 2004 to 2006, two clinical studies showed the "efficacy and safety of combining metformin with DPP-IV inhibitors." (Tr. 520:1-3 (Accili)). Finally, even when a DPP-IV inhibitor and metformin are given together, the same standard doses for metformin that are found in prior art will be used. This Court finds that here, it is not a distinction to claim those previously disclosed metformin

dosages. Accordingly, this Court finds that the asserted claims and the references are not patentably distinct.

In response, Boehringer argues that Defendant's improperly relied on hindsight analysis in relying on the '510 publication's preferred dosage range. Court's may not rely on hindsight bias in determining whether a patent is invalid for obviousness-type double patenting or obviousness. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007) ("factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning"). "[T]he inventor's own path itself never leads to a conclusion of obviousness; that is hindsight. What matters is the path that the person of ordinary skill in the art would have followed, as evidenced by the pertinent prior art." *Millennium Pharm., Inc. v. Sandoz Inc.*, 862 F.3d 1356, 1367 (Fed. Cir. 2017) (citations omitted).

Here, the reference claims recite a "pharmaceutically effective amount" of linagliptin in combination with metformin for treating type 2 diabetes. However, the reference claims do not disclose a dose for either linagliptin or metformin. Instead, the '510 publication, a known prior art that a POSA would have relied upon, specifically discloses the preferred 1-100mg dose range. A POSA is presumed to have knowledge of prior art available; accordingly, a POSA is presumed to have been aware of the '510 publication. Here, it is not hindsight that informs the path a POSA would take, instead that path is informed by "pertinent prior art" that a POSA would follow; i.e. the '510 publication. *See Millennium Pharm, Inc.*, 863 F.3d at 1357.

iii. Conclusion of Obvious-type Double Patenting

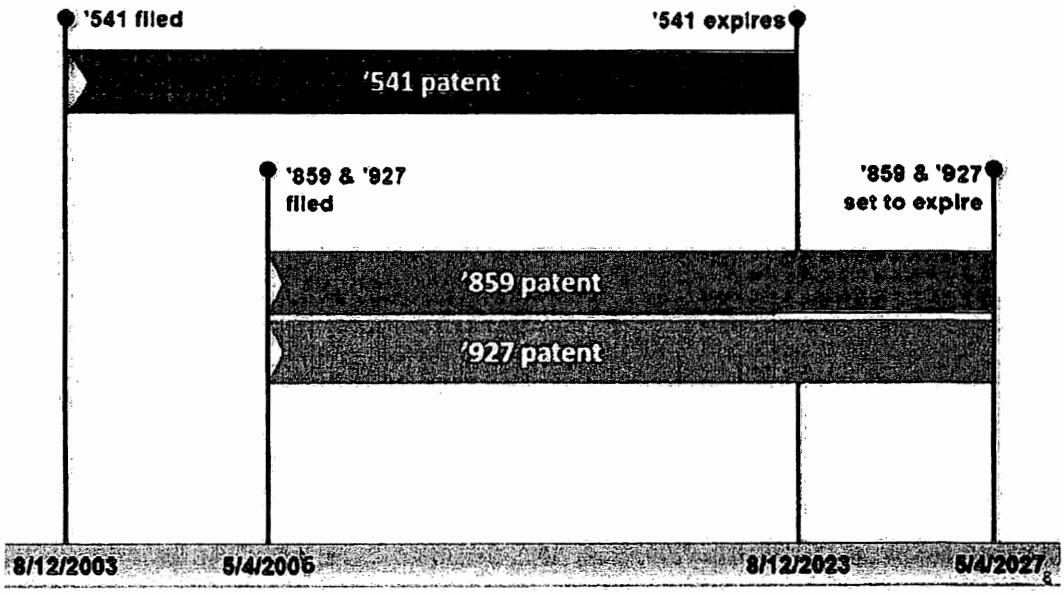
In summary, Boehringer's '541 Patent expires on August 12, 2023, and claims a method of treating type 2 diabetes with a "pharmaceutically effective amount" of linagliptin and

metformin, as well as a pharmaceutical composition containing linagliptin and metformin. (Defs. PFoF at ¶ ¶ 411 to 414). In contrast, the Asserted Patents expire on May 4, 2027, almost four years later, and claim compositions and methods of treating type 2 diabetes with 2.5 or 5 mg of linagliptin and standard doses of metformin, or no metformin at all, in oral doses. (Defs. PFoF at ¶¶ 135; 139–146; 150; 153–158; 412; 415). The first step in the obviousness-type double patenting analysis requires comparing the asserted claims to the reference claims; here, the only differences between the asserted claims and the reference claims are that the asserted claims disclose specific dosages for linagliptin and metformin, and that these drugs may be taken orally. The second step requires determining whether these differences render the asserted claims patentably distinct. In this regard, the Defendant's have shown, by clear and convincing evidence, that the asserted claims are not patentably distinct from the reference claims.

Regarding the oral administration of the drugs, the '510 publication and Glucophage label clearly discloses that the drugs may be taken orally. Regarding linagliptin dosages, the '510 publication discloses a dosage for DPP-IV inhibitors in a range "preferably 1 to 100mg." Second, the '510 publication discloses that linagliptin is one of thirty of the "most particularly preferred" compounds disclosed. Third, the '510 publication discloses that linagliptin is one of the most potent compounds disclosed, with an IC_{50} value of 1nM. Fourth, based on the disclosed range of 1 to 100mg and linagliptin's disclosed potency, a POSA would be motivated to conduct a dose ranging study and, through routine scientific experimentation, arrive at the asserted claims linagliptin dose of 2.5mg to 5mg. Regarding metformin dosages, several prior arts disclose the dosage of metformin. The chart below summarizes the prior arts' disclosures of both linagliptin and metformin dosages.

Reference	Method of Treating T2D	Linagliptin Dose	Metformin Dose
510 Publication	"for the prevention or treatment of ... type II diabetes mellitus" JTX-011.0002	"preferably 1 to 100mg" JTX-011.0013	
Glucophage	"management of type 2 diabetes" DTX-039_0001		"500 mg twice a day or 850 mg once a day" DTX-039_0025
Ahren	"Effectively prevents deterioration of glycemic control when added to metformin monotherapy in type 2 diabetes" JTX-012.0001		"1,500-3,000 mg/day" JTX-012.0001
Hughes	"effective in treatment of type 2 diabetes" JTX-015.0003		"Preferably from about 500 mg to about 2000 mg" JTX-015.0023

The claimed differences between the asserted claims and the reference claims are not patentably distinct, as the differences between these claims are disclosed in prior art. Accordingly, the asserted claims do not reveal any new invention. Through the asserted claims, Boehringer has attempted to extend the '541 patent an additional four years through the '927 and '859 patent – exactly the type of behavior that the obviousness-type double patenting doctrine seeks to prevent. *See Gilead Scis., Inc.*, 753 F.3d at 1212; *Sun Pharm. Indus.*, 611 F.3d at 1384.



If this Court were to ignore Boehringer's attempt to extend the life of its '541 patent, it would allow Boehringer the ability to control the right of the public, and Defendants, to use linagliptin and metformin "far beyond the term awarded to him under the patent laws." *Gilead Scis., Inc.*, 753 F.3d at 1212. Accordingly, this Court finds that the asserted claims 7, 9, 15, 17, 19, 25, and 26 in the '927 patent and the asserted claims 1, 14, 15, 20, and 21 in the '859 patent are invalid for obviousness-type double patenting.

b. The asserted claims are invalid for obviousness.

A patent may be invalidated if the subject matter of the patent is obvious. A patent may not be obtained "if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains." 35 U.S.C. § 103(a). Obviousness is a question of law based on underlying factual findings concerning: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claims and the prior art; and (4) secondary considerations of non-obviousness, such as commercial success, long felt but unsolved need, failure of others, acquiescence of others in the industry that the patent is valid, and unexpected results. *See KSR Int'l Co.*, 550 U.S. at 405 (quoting *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 86 S. Ct. 684, 15 L. Ed. 2d 545 (1966)). "Although secondary considerations must be taken into account, they do not necessarily control the obviousness conclusion." *In re Huai-Hung Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011) (quoting *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1372 (Fed. Cir. 2007)).

"[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *See KSR Int'l Co.*, 550 U.S. at 418; *see also Unigene Labs., Inc. v. Apotex, Inc.*, 655 F.3d 1352, 1360 (Fed. Cir. 2011). Instead,

proof of obviousness requires proof that a POSA "would have had reason to combine the teaching of the prior art references to achieve the claimed invention, and . . . would have had a reasonable expectation of success from doing so." *In re Cyclobenzaprine*, 676 F.3d 1063, 1069 (Fed. Cir. 2012), *cert. denied*, 133 S. Ct. 933, 184 L. Ed. 2d 725 (U.S. 2013) (citing *Procter & Gamble*, 566 F.3d at 994); *see also Amgen Inc. v. F. Hoffmann-La Roche, Ltd.*, 580 F.3d 1340, 1362 (Fed. Cir. 2009) ("An obviousness determination requires that a skilled artisan would have perceived a reasonable expectation of success in making the invention in light of the prior art."). Such a person would interpret prior art references "using common sense and appropriate perspective." *Unigene Labs., Inc. v. Apotex, Inc.*, 655 F.3d 1352, 1361 (Fed. Cir. 2011).

While an analysis of any teaching, suggestion, or motivation to combine known elements is useful to an obviousness analysis, the overall obviousness inquiry must be expansive and flexible. *See KSR Int'l Co.*, 550 U.S. at 415, 419. In addition, the use of hindsight is not permitted when determining whether a claim would have been obvious to one of ordinary skill in the art. *See id.* at 421 (cautioning against "the distortion caused by hindsight bias" and obviousness "arguments reliant upon ex post reasoning"). However, the court can "take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at 418. "One of the ways in which a patent's subject matter can be proved obvious is by noting that there existed at the time of invention a known problem for which there was an obvious solution encompassed by the patent's claims." *Id.* at 419-20. Accordingly, an invention may be obvious where "there [was] . . . a design need or market pressure to solve a problem and there [were] . . . a finite number of identified, predictable solutions." *Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd*, 533 F.3d 1353, 1359 (Fed. Cir. 2008) (citations omitted). "[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." *KSR Int't. Co.*, 550 U.S. at 420.

A prima facie case may be rebutted "where the results of optimizing a variable, which was known to be result effective, are unexpectedly good." *In re Applied Materials, Inc.*, 692 F.3d 1289, 1295 (Fed. Cir. 2012). However, evidence of a "finite number of identified, predictable solutions" or alternatives "might support an inference of obviousness." *See Eisai Co. Ltd. v. Dr. Reddy's Labs. Ltd.*, 533 F.3d 1353, 1359 (Fed. Cir. 2008) (citation omitted). Accordingly, "obviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007).

An obviousness analysis is analogous to an obviousness-type double-patenting analysis under 35 U.S.C. § 103. *Abbvie Inc.*, 764 F.3d at 1378. However, there are three distinctions between the obviousness analysis and the obvious for double patenting analysis:

> First, statutory obviousness compares claimed subject matter to the prior art, while non-statutory double patenting compares claims in an earlier patent to claims in a later patent or application. Second, double patenting does not require inquiry into a motivation to modify the prior art. Finally, double patenting does not require inquiry into objective criteria suggesting non-obviousness.
>
> *P&G v. Teva Pharm. USA, Inc.*, 566 F.3d 989, 999 (Fed. Cir. 2009)

In contrast with the obviousness-type double patenting analysis, this Court begins its obviousness analysis with the prior art as the starting point, and not the reference claims. Essentially, all of the discussion above in the context of obviousness-type double patenting applies equally with respect to obviousness. This Court must determine if the asserted claims are rendered obvious in light of the prior art, and whether a POSA would have been motivated to combine the teachings from the prior art, and achieve the claimed invention of the asserted claims. For the following reasons, this Court finds the asserted claims are obvious considering the prior art.

First, as stated above, the '510 Publication discloses linagliptin.[11] (*See* JTX 11.0057 at ¶ 2400). While the '510 publication also discloses approximately 7,000 other DPP-IV inhibitors, it highlights linagliptin in two separate areas. The '510 Publication lists linagliptin as one of the thirty most particularly preferred compounds, and it lists linagliptin as having an IC_{50} value of 1nM, noting that linagliptin was exceptionally potent. (JTX-11.0009, at ¶¶ 232, 245; JTX-11.0013). The '510 publication also disclosed a dose range of 1-100mg for all of the compounds disclosed in the publication. (JTX-11.0013). Based on the combination of those factors, a POSA would have been motivated to select linagliptin from the '510 publication, and begin a dose ranging study.

Here, the claimed invention's doses of linagliptin in 2.5 mg and 5 mg fall within the '510 publications disclosed range of 1-100mg. Accordingly, there is a presumption of obviousness. *See Tyco Healthcare Grp. LP*, 642 F.3d at 1372–73 (quoting *Iron Grip Barbell Co.*, 392 F.3d at 1322). Further, the evidence adduced at trial showed that a POSA would have been motivated to begin a dose ranging study at the low end of the range, or at 75mg and divide by some number, due to linagliptin's high potency and the prior art available at the time. (*See* JTX-16.0023 at ¶ 234; (Tr 725:21–726:6; Tr. 752:15 – 18 (Grass)); (JTX-013); (Tr. 1464:11-17; 1476:4 to 1477-16 (Dugi)). Boehringer agues that there are other factors that would motivate a POSA to select a compound from the '510 publication, and that a POSA would not simply ignore the Examples in the '510 publication that recites specific doses for the DPP-IV inhibitors disclosed in the

[11] There are also issues as to whether a POSA would be motivated to select linagliptin to treat diabetes; and whether a POSA would have administered linagliptin and metformin orally. First, the '510 publication specifically states that the DPP-IV inhibitors that it discloses can be used for treating type 2 diabetes. *See* Dfs. PFoF at ¶¶ 332-334. Second, both the '510 publication and the Glucophage labels state that the drugs may be administered orally through tablets. *See* JTX-11.13, ¶ 300; JTX-11.67-.68; DTX-39.1).

publication. However, as this Court previously noted, examples must be read as part of the publication as a whole, and it is impermissible to choose any one example or reference in order to support a given position to the "exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art." *Bausch & Lomb, Inc.*, 796 F.2d at 448. Boehringer's actions of holding out the '510 publication's examples does exactly this.

Boehringer further argues that the potency of linagliptin disclosed in the '510 publication has minimal value, as such a value is determined from an *in vitro* test, and does not relate to what an appropriate human dose should be, or how a drug would behave *in vivo*. (Tr. 81:12-18 (Mark); Tr. 1008:12-18 (Lam)). However, Boehringer's experts, through Dr. Lam, agreed that the '510 publication itself does not "provide much information in terms of what's happening in a biological system" of a human, i.e., how the disclosed compounds would behave *in vivo*. (Tr. 1035:11-15) (Lam)). For the purposes of the obviousness analysis for the issues before this Court, is irrelevant that a IC_{50} value does not provide information on how a drug will interact *in vivo*, where the '510 publication does not disclose any *in vivo* information. Instead, the disclosure of the IC_{50} value and high potency of linagliptin is a motivating factor to begin dose ranging studies and *in vivo* testing. Taking the '510 publication as a whole, in light of its teachings that linagliptin is highly potent and its status one of the "most particularly preferred" DPP-IV inhibitors, the Court finds a POSA would have been motivated to select linagliptin from the '510 publication, and begin a dose-ranging studies.

Second, the metformin dosages, and that metformin could be combined with DPP-IV inhibitors like linagliptin, were disclosed in prior art. Specifically, the Glucophage label, the Ahren article, and the Hughes international patent application each disclose dosages of metformin, which are the same or substantially similar to the dosages disclosed in the asserted claims. (*See*

DTX-39; JTX.15.2-.3, .23; JTX-12.1; Tr. 535:2-4; Tr. 503:17-22 (Accili)). Accordingly, the Court finds a POSA would have been motivated to combine metformin, at its disclosed doses, with linagliptin.

Here, as in *KSR*, a POSA would have been motivated to fit the teachings of the '510 publication together, along with other prior art, to reach the patented invention, i.e., the asserted claims. *KSR Int'l Co.*, 550 U.S. at 420. Accordingly, for the same reasons expressed in the Court's obvious-type double patenting analysis, this Court finds that the asserted claims 7, 9, 15, 17, 19, 25, and 26 in the '927 patent and the asserted claims 1, 14, 15, 20, and 21 in the '859 patent are invalid for obviousness.

B. Boehringer has not set forth any Secondary Considerations to overcome the presumption of obviousness.

"Once a *prima facie* case of obviousness has been established, the burden shifts to the applicant to come forward with evidence of nonobviousness [or secondary considerations] to overcome the *prima facie* case." *In re Huang*, 100 F.3d 135, 139 (Fed. Cir. 1996). Secondary considerations can include unexpected results created by the claimed invention, a long-felt but unmet need, and evidence of commercial success. *See Aventis Pharma S.A. v. Hospira, Inc.*, 743 F. Supp. 2d 305, 344 (D. Del. 2010) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1996)). "Although secondary considerations must be taken into account, they do not necessarily control the obviousness conclusion." *Pfizer*, 480 F.3d at 1372. Instead, in order to give substantial weight to secondary considerations, "[a] nexus between the merits of the claimed invention and evidence of secondary considerations is required[.]" *Muniauction, Inc. v. Thomson Corp.*, 532 F.3d 1318, 1327 (Fed. Cir. 2008). "Put another way, commercial success or other secondary considerations may presumptively be attributed to the patented invention only where 'the marketed product embodies the claimed features, and is coextensive with them.'" *Id.* at 1328 (quoting *Ormco Corp.*

v. Align Tech., Inc., 463 F.3d 1299, 1311-12 (Fed. Cir. 2006)). "Where a claimed invention represents no more than the predictable use of prior art elements according to established functions, . . . evidence of secondary indicia are frequently deemed inadequate to establish non-obviousness." *Ohio Willow Wood Co. v. Alps S., LLC*, 735 F.3d 1333, 1344 (Fed. Cir. 2013) (citing *Western Union Co. v. MoneyGram Payment Sys., Inc.*, 626 F.3d 1361, 1373 (Fed. Cir. 2010) ("weak secondary considerations generally do not overcome a strong prima facie case of obviousness")).

1. Unexpected results

To rebut a prima facie case of obviousness, a patent applicant may show unexpected results, that "there is a difference between the results obtained and those of the closest prior art, and that the difference would not have been expected by one of ordinary skill in the art at the time of the invention." *Bristol-Myers Squibb Co. v. Teva Pharm. USA, Inc.*, 752 F.3d 967, 977 (Fed. Cir. 2014) (citing *Kao Corp. v. Unilever U.S., Inc.*, 441 F.3d 963, 970 (Fed. Cir. 2006)). This can be shown when "the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected." *Procter & Gamble Co. v. Teva Pharm. USA, Inc.*, 566 F.3d 989, 994 (Fed. Cir. 2009). "In order to properly evaluate whether a superior property was unexpected, the court should [] consider[] what properties were expected." *Pfizer*, 480 F.3d at 1371. "Unexpected results that are probative of non-obviousness are those that are "different in kind and not merely in degree from the results of the prior art. Results which differ by percentages are differences in degree rather than kind, where the modification of the percentage is within the capabilities of one skilled in the art at the time." *Galderma Labs., L.P.*, 737 F.3d at 739 (quoting *Iron Grip Barbell Co.*, 392 F.3d at 1322).

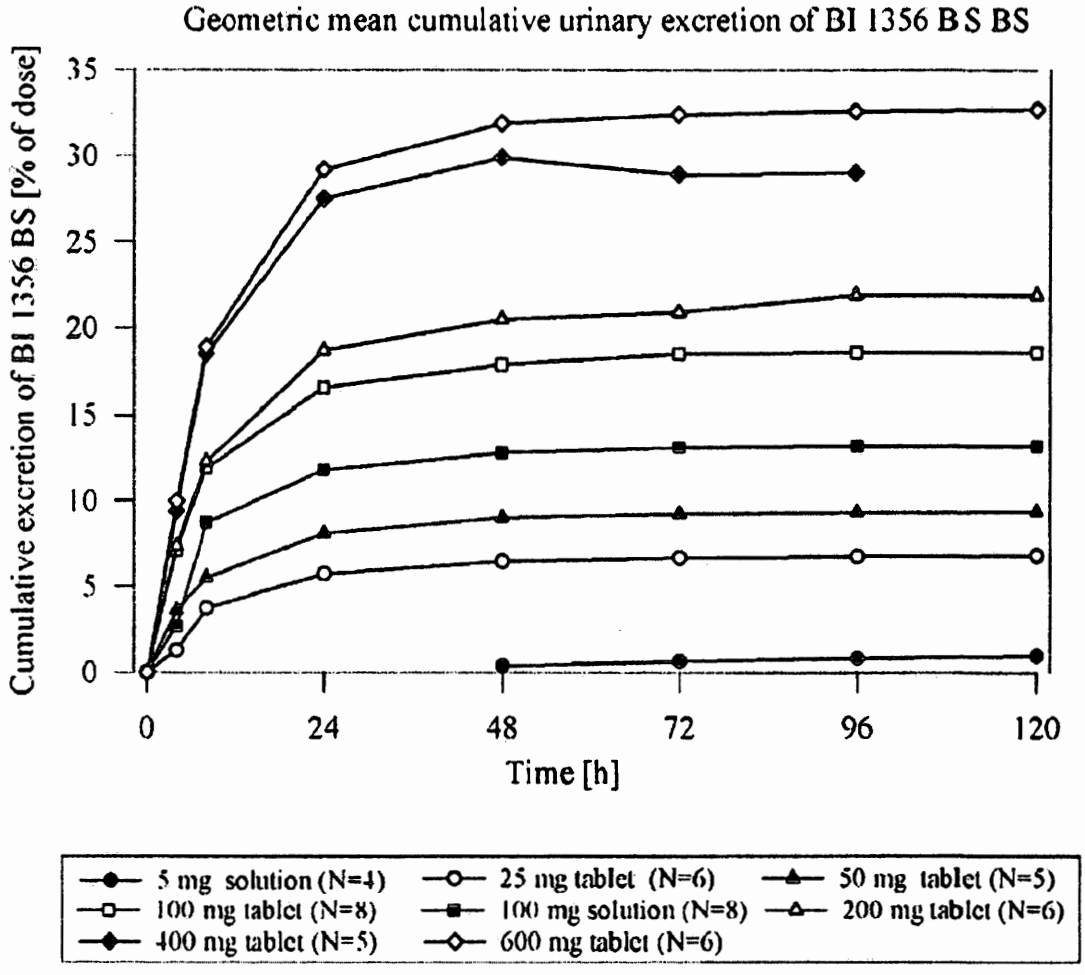
Boehringer argues that the unexpected result here was linagliptin clearing through the body hepatically (i.e., through the liver) as opposed to renally (i.e., through the kidneys). In response,

Defendants argue that there was no unexpected result because a POSA would have no expectation about how the body would clear linagliptin. Boehringer offers no evidence which supports that the renal clearance of linagliptin was an unexpected result. Instead, at trial Boehringer's expert Dr. Lenhard confirmed that as of the priority date, a POSA would not have had any expectation about how linagliptin was excreted from the body. (*See* Tr. 956:22 to 957:2 ("Q. What about as of May of 2006, would a POSA had an expectation of how linagliptin would be excreted; and your answer was? A. As of 2006 I don't think a POSA would have an expectation because the excretion method was not clearly known at that time."). (Defs. PFoF at ¶ 446). Moreover, Dr. Mark explained Boehringer did not have any expectation regarding how linagliptin would be excreted through the body, and that linagliptin was not chosen based on any potential properties relating to renal excretion. (Tr. 118:7-13 (Mark)).

As such, Dr. Accili explained, and this Court agrees, that a POSA would not have an expectation on how linagliptin would be excreted because "each compound, each molecule has to be evaluated on its...own, its own properties. And linagliptin was different from other DPP-IV inhibitors . . . So we have every reason to think that one should evaluate linagliptin before coming to a conclusion one way or another. There's no way one can predict how is the drug going to be excreted by the body, it an empirical finding." (Accili (1350:25-1351:10).)

Defendants also argue that linagliptin's renal excretion properties show only a difference in degree, and not in kind from the claimed doses when compared to other unclaimed doses, and thus, Boehringer has failed to come forth with any evidence of unexpected results. Defendants first point to the Tradjenta label, which recites that for 5mg of linagliptin, 5% is cleared through the kidney. (PTX-8.6). Defendants next point to the following graph, which shows for a 25mg

tablet, still 5% is cleared through the kidney, and for a 50mg tablet, 7% is cleared through the kidney.



Here, the differences between the claimed 5mg tablet excretion, and the 25mg and 50mg tablets excretions are minimal. Between a 5mg and 25mg tablet, there is no difference at all in urinary excretion. Between, the 5mg and 50mg tablet, there is only a 2% difference in urinary excretion. Accordingly, they are do not demonstrate a difference in kind, necessary to show unexpected results. *See In re Harris*, 409 F.3d 1339, 1344 (Fed. Cir. 2005); *see also In re Huang*, 100 F.3d 135, 139 (Fed. Cir. 1996) (claimed ranges must "produce a new and unexpected result

which is different in kind and not merely in degree from results of the prior art"). Accordingly, Boehringer has not shown how linagliptin's renal excretion was an unexcepted result.

2. Unmet need

To show a long-felt, but unmet need, a patentee must show "an articulated identified problem and evidence of efforts to solve that problem." *Tex. Instruments, Inc. v. United States ITC*, 988 F.2d 1165, 1178 (Fed. Cir. 1993). There must be a nexus between the "novel feature of the [claimed invention] and the long-felt, unmet need." *AstraZeneca LP v. Breath Ltd.*, 88 F. Supp. 3d 326, 388–89 (D.N.J.), *aff'd*, 603 F. App'x 999 (Fed. Cir. 2015); *See also Cubist Pharm., Inc. v. Hospira, Inc.*, 75 F. Supp. 3d 641, 672 (D. Del. 2014), *aff'd*, 805 F.3d 1112 (Fed. Cir. 2015) (finding no nexus between alleged long-felt need and novel features of the claimed invention).

This Court looks to the effective filing date, here May 4, 2006, to determine if, at that time, there was a long-felt, but unmet need for the asserted claims. Here, Boehringer argues that a long-felt, but unmet need existed for a drug that does not require a dose adjustment, and that is not contraindicated in patients with a renal insufficiency. "Establishing a long-felt need requires a showing that others skilled in the art in fact perceived a need and that this perception persisted over a long period of time without resolution by the prior art." *Markman v. Lehman*, 987 F. Supp. 25, 43 (D.D.C. 1997). Boehringer points to its own internal document titled "Production Development Plan," dated April 4, 2004, that states that "there is current unmet medical need with regard to the safety profile" for a drug that "is not contraindicated in patients with renal insufficiency." (PTX-252.38.) It adds that "the best case scenario to improve unmet medical need would be a compound with," among other features, "[s]uperior safety profile . . . in patients with renal failure." (PTX-252.38). Apart from its own internal documents, Boehringer has not shown that any POSA perceived a need for a drug that does not require dose adjustment, or is

contraindicated in patients with a renal insufficiency. Boehringer's own internal documents are not the equivalent to a POSA recognizing such a long-felt, yet unmet need.

Boehringer also points to the lack of DPP-IV inhibitors that were not contraindicated for type-2 diabetes patients with renal failure. Boehringer argues that several other DPP-IV inhibitors are primarily renally excreted (Vildagliptin, Alogliptin and Saxagliptin.) and thus a need existed for a DPP-IV inhibitor with a low renal excretion level. However, evidence of these DPP-IV inhibitors is post-priority evidence, as Vildagliptin, was first approved in Australia on March 2, 2010 (PTX-144.2). Alogliptin was initially approved in the United States in 2013 (PTX-145.1), and Saxagliptin was initially approved in the United States in 2009 (PTX-592.1). These DPP-IV inhibitor's renal excretion levels were not known to a POSA at the time of the effective filing date, and are thus not relevant to this Court's analysis for secondary considerations of obviousness.

Further, at the time of the effective filing date, other drugs were available to treat type 2 diabetic patients suffering from renal impairment, and that could also be used without dose adjustments. Dr. Accili explained that well before the priority date, a POSA would know that TZD's could be used for patients who suffered from renal impairment, without dose adjustment. (Tr. 1334:17-23) (Accili)). Dr. Accili stated TZDs could be used "safely and effectively . . . in diabetic patients that had poor kidney function[, and] at the time of the priority date, they were widely used in patients with diabetes and they did not require dose adjustment with renal impairment." (Tr. 1334:17-1335:5 (Accili)). Dr. Accili also explained that none of the asserted claims recite anything related to renal excretion, and none of the specifications from the asserted patents recite anything related to renal excretion, thus, there was no nexus between the asserted claims of the patents-in-suit and the secondary consideration of long-felt but unmet need. (Tr. 1340:1-15 (Accili)).

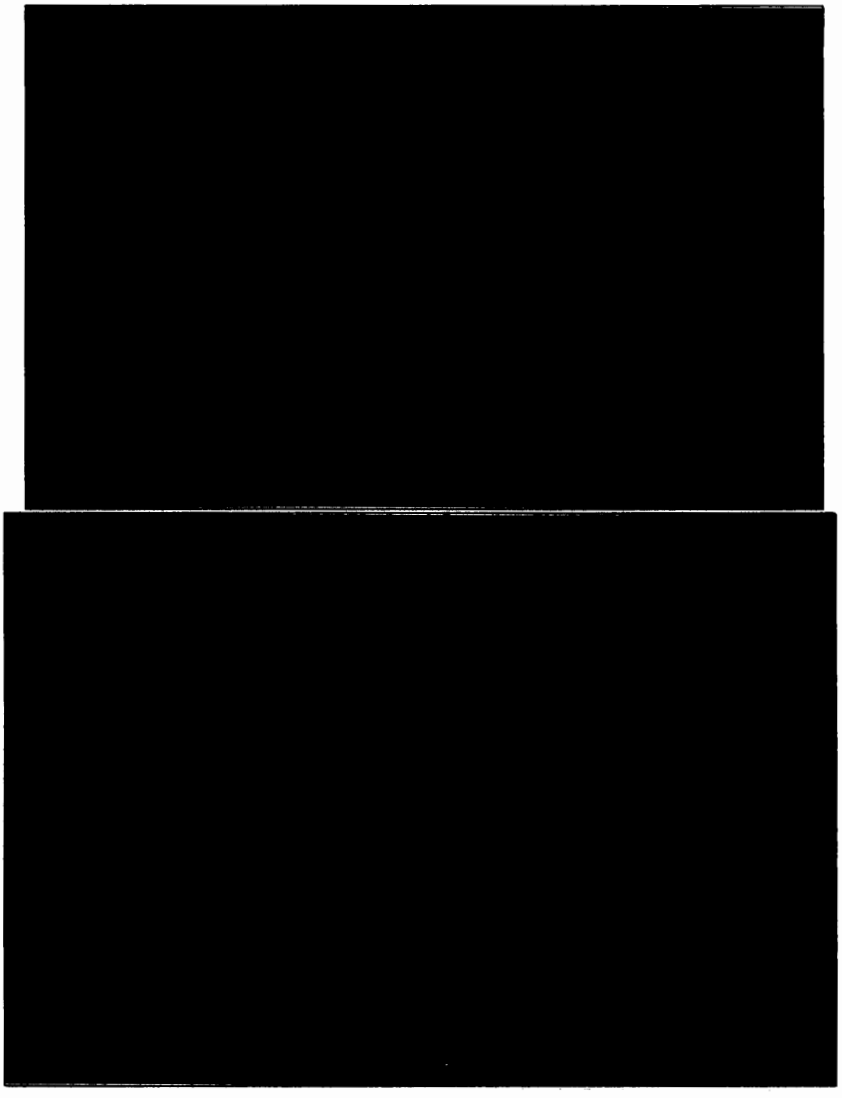
In summary, Boehringer cites to no evidence that would show these needs were long-felt, or that others skilled in the art considered these needs significant. Instead, Boehringer relies on its own internal documents to show that there was a long-felt and unmet need; however, these internal documents do not show that a POSA also perceived a long-felt, yet unmet need. Further, Boehringer's reliance on other DPP-IV renal clearance amounts is misplaced, as these drugs first became available after the priority date. There were other drugs available at the time, specifically TZDs, that could be used safely and effectively for patients with type 2 diabetes. Finally, Boehringer's arguments reflecting that the presumption of obviousness should be rebutted due to an unmet, yet long-felt need for a therapeutically effective drug that can treat type 2 diabetes in patients with renal impairment and without requiring dose adjustments is rebutted by Boehringer's own contentions. Here, Boehringer admits that the most important aspect of the asserted claims is not linagliptin's effectiveness in treating patients with renal impairment, but the actual doses found in the asserted claims. During closing arguments, Boehringer's counsel clarified: "[Y]ou know what; if they want to sell linagliptin at 10 milligrams, these patents don't stop them. If they want to sell linagliptin at 25 milligrams, these patents don't stop them." (Tr. 1600:8-11). Accordingly, Boehringer has not demonstrated that there was a long-felt, but unmet need, and in this respect, has not overcome the presumption of obviousness.

3. Commercial success

Courts may consider evidence of commercial success of a claimed invention in the secondary consideration analysis. *See Graham*, 383 U.S. at 17. "Commercial success is relevant to obviousness only if there is a 'nexus . . . between the sales and the merits of the claimed invention.'" *In re Applied Materials, Inc.*, 692 F.3d 1289, 1299-300 (Fed. Cir. 2012) (quoting *In re Huang*, 100 F.3d at 140). "There must be 'proof that the sales were a direct result of the unique

characteristics of the claimed invention—as opposed to other economic and commercial factors unrelated to the quality of the patented subject matter.'" *Id.* (quoting *In re Huang*, 100 F.3d at 140). Additionally, "evidence related solely to the number of units sold provides a very weak showing of commercial success, if any." *In re Huang*, 100 F.3d at 140 (listing cases). "Just as the number of units sold without evidence of the market share is only weak evidence of commercial success, so too is an assertion of market share lacking in sales data." *In re Applied Materials, Inc.*, 692 F.3d at 1300 (citation omitted). "The more probative evidence of commercial success relates to whether the sales represent 'a substantial quantity in th[e] market.'" *Id.* (quoting *In re Huang*, 100 F.3d at 140). Courts have found a no commercial success where sales of the patented drug "were dwarfed" by those of other drugs in the market and "fell short of [the patentee's] own expectations." *See Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1357 (Fed. Cir. 2012).

Boehringer argues that the asserted claims commercial success is shown through examining the total prescriptions written by physicians for both Tradjenta® and Jentadeuto®. Boehringer's expert, Dr. Schwartz, testified that [redacted]" (Tr. 1151:20 to 1152:2 (Schwartz)). Dr. Blackburn confirmed that Tradjenta's® volume of prescriptions [redacted]. (PFF 825; Tr. 1329:5-11 (Blackburn)). Dr. Schwartz explained, "Since their approval both [Tradjenta® and Jentadueto®] [have] won substantial business, they've been able to sustain their gains, they've gained market share, they've taken business away from their rivals, all of which are indicia and supportive of a finding of commercial success." (Tr. 1134:22-1135:2 (Schwartz).)



Defendants counter and offer evidence that both Tradjenta® and Jentadueto® have not been commercially successful, and have been dwarfed by market competitor Januvia. Defendants point to internal Boehringer documents which projected sales forecasts for both Tradjenta® and Jentadueto®, and the actual net sales, which showed the Sales for Tradjenta® and Jentadueto®

(DFF 497).

[redacted] Thus, Boehringer has provided, at best, evidence of a modest level of commercial success for Tradjenta® and Jentadueto®. Accordingly, this evidence is insufficient to overcome a presumption of obviousness.

III

Conclusion

After careful consideration of the entire record in this case in light of the applicable law, the Court hereby concludes that: (1) Defendants have proved by clear and convincing evidence that the asserted claims of the '859 and '927 patents are invalid for obvious-type double patenting; (2) Defendants have proved by clear and convincing evidence that the asserted claims of the '859 and '927 patents are invalid as obvious; and (3) Boehringer has failed to show any evidence non-obviousness [or secondary considerations] to overcome the *prima facie* case of obviousness. Because the asserted claims are invalid for obvious-type double patenting and for obviousness, this court need not reach the issues of invalid for anticipation or infringement.[12]

PETER G. SHERIDAN, U.S.D.J.

[12] *See Commil USA, LLC*, 135 S. Ct. 1920, 1929 (2015) ("To say that an invalid patent cannot be infringed, or that someone cannot be induced to infringe an invalid patent, is in one sense a simple truth, both as a matter of logic and semantics. . . To be sure, if at the end of the day, an act that would have been an infringement or an inducement to infringe pertains to a patent that is shown to be invalid, there is no patent to be infringed."); *Richdel, Inc. v. Sunspool Corp.*, 714 F.2d 1573, 1580 (Fed. Cir. 1983) ("The claim being invalid there is nothing to be infringed.); *see also Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, 411 F.3d 1332, 1339-40 (Fed. Cir. 2005).